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=> file registry
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.21       0.21

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STRUCTURE FILE UPDATES:   22 OCT 2007  HIGHEST RN 951207-62-8
DICTIONARY FILE UPDATES:  22 OCT 2007  HIGHEST RN 951207-62-8

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TSCA INFORMATION NOW CURRENT THROUGH June 29, 2007

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  conducting SmartSELECT searches.

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predicted properties as well as tags indicating availability of
experimental property data in the original document.  For information
on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=> s risperidone/cn
L1            1 RISPERIDONE/CN

=> d l1

L1   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2007 ACS on STN
RN   106266-06-2  REGISTRY
ED   Entered STN:  24 Jan 1987
CN   4H-Pyrido[1,2-a]pyrimidin-4-one, 3-[2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-
     1-piperidinyl]ethyl]-6,7,8,9-tetrahydro-2-methyl-  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   1,2-Benzisoxazole, 4H-pyrido[1,2-a]pyrimidin-4-one deriv.
OTHER NAMES:
CN   R 64766
CN   Rispadal
CN   Risperdal
CN   Risperidal
CN   Risperidone
CN   Spiron
MF   C23 H27 F N4 O2
CI   COM
SR   CA
LC   STN Files:   ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOSIS,
       BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CHEMCATS, CIN, CSCHEM, DDFU,
       DRUGU, EMBASE, IMSCOSEARCH, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA,
       MEDLINE, MRCK*, PATDPASPC, PHAR, PROMT, PROUSDDR, PS, RTECS*, SYNTHLINE,
       TOXCENTER, USAN, USPAT2, USPATFULL
         (*File contains numerically searchable property data)
     Other Sources:   WHO
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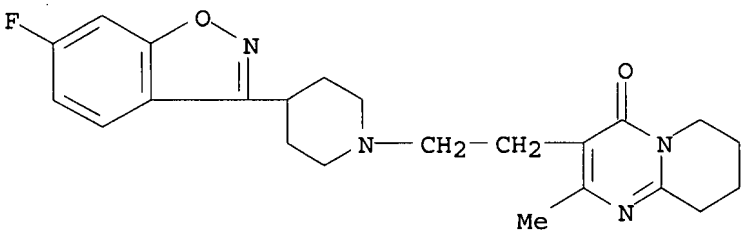


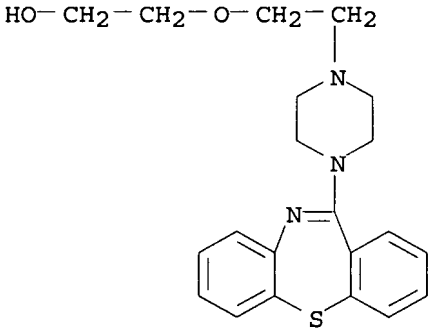
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2373 REFERENCES IN FILE CA (1907 TO DATE)
13 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
2385 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> s quetiapine/cn
L2 1 QUETIAPINE/CN

=> d l2

L2 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2007 ACS on STN
RN 111974-69-7 REGISTRY
ED Entered STN: 19 Dec 1987
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-
(CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Dibenzo[b,f][1,4]thiazepine, ethanol deriv.
OTHER NAMES:
CN Quetiapine
DR 264256-90-8
MF C21 H25 N3 O2 S
CI COM
SR CA
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BIOSIS, CA, CAPLUS, CASREACT, CBNB, CHEMCATS, CIN, DDFU, DRUGU, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, MRCK*, PATDPASPC, PHAR, PROMT, PROUSDDR, PS, RTECS*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

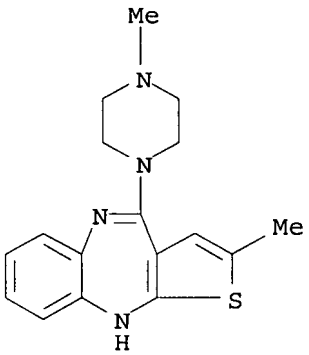
916 REFERENCES IN FILE CA (1907 TO DATE)
13 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
925 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> s olanzapine/cn
L3 1 OLANZAPINE/CN

=> s l3
L4 1 OLANZAPINE/CN

=> d l4

L4 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2007 ACS on STN
RN 132539-06-1 REGISTRY
ED Entered STN: 08 Mar 1991
CN 10H-Thieno[2,3-b][1,5]benzodiazepine, 2-methyl-4-(4-methyl-1-piperazinyl)-
(CA INDEX NAME)
OTHER NAMES:
CN Lanzac
CN LY 170053
CN Olanzapine
CN Zyprexa
MF C17 H20 N4 S
CI COM
SR US Adopted Names Council (USAN)
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CHEMCATS, CIN, CSCHEM, DDFU, DRUGU, EMBASE, IMSCOSEARCH, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, MEDLINE, MRCK*, PATDPASPC, PHAR, PIRA, PROMT, PROUSDDR, PS, RTECS*, SCISEARCH, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)



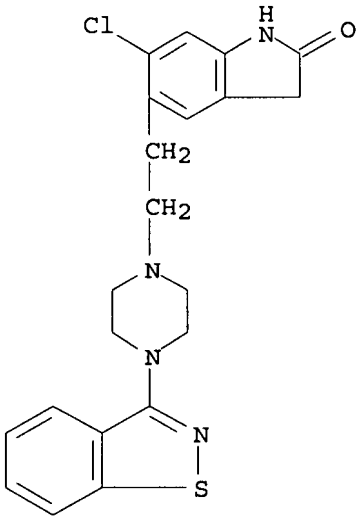
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2192 REFERENCES IN FILE CA (1907 TO DATE)
25 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
2201 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> s ziprasidone/cn
L5 1 ZIPRASIDONE/CN

=> d l5

L5 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2007 ACS on STN
RN 146939-27-7 REGISTRY
ED Entered STN: 13 Apr 1993
CN 2H-Indol-2-one, 5-[2-[4-(1,2-benzisothiazol-3-yl)-1-piperazinyl]ethyl]-6-chloro-1,3-dihydro- (CA INDEX NAME)
OTHER NAMES:
CN 5-[2-[4-(1,2-Benzisothiazol-3-yl)-1-piperazinyl)ethyl]-6-chloro-1,3-dihydro-2H-indol-2-one
CN 5-[2-[4-(1,2-Benzisothiazol-3-yl)-1-piperazinyl]ethyl]-6-chloro-2-indolinone
CN 5-[2-[4-(Benzo[d]isothiazol-3-yl)piperazin-1-yl]ethyl]-6-chloro-1,3-dihydroindol-2-one
CN CP 88059
CN Geodon
CN Zaprasidone
CN Ziprasidone
MF C21 H21 Cl N4 O S
CI COM
SR World Health Organization (WHO)
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BIOSIS, CA, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMLIST, CIN, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, MEDLINE, MRCK*, PATDPASPC, PHAR, PROMT, PROUSDDR, PS, RTECS*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: WHO



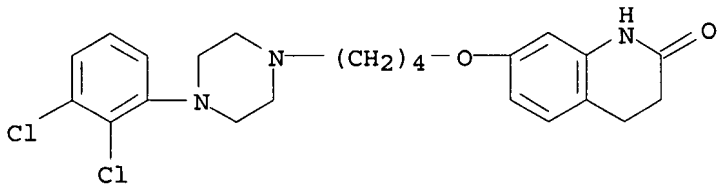
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

704 REFERENCES IN FILE CA (1907 TO DATE)
13 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
707 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> s aripiprazole/cn
L6 1 ARIPIPRAZOLE/CN

=> d l6

L6 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2007 ACS on STN
RN 129722-12-9 REGISTRY
ED Entered STN: 05 Oct 1990
CN 2(1H)-Quinolinone, 7-[4-[4-(2,3-dichlorophenyl)-1-piperazinyl]butoxy]-3,4-dihydro- (CA INDEX NAME)
OTHER NAMES:
CN 7-[4-[4-(2,3-Dichlorophenyl)-1-piperazinyl]butoxy]-3,4-dihydrocarbostyril
CN Abilify
CN Abilitat
CN Aripiprazole
CN OPC 14597
CN OPC 31
DR 156680-99-8
MF C23 H27 Cl2 N3 O2
CI COM
SR CA
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CHEMCATS, CIN, CSCHEM, DDFU, DRUGU, EMBASE, HSDB*, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, MEDLINE, MRCK*, PATDPASPC, PHAR, PROMT, PROUSDDR, PS, RTECS*, SCISEARCH, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL
(*File contains numerically searchable property data)
Other Sources: WHO



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

548 REFERENCES IN FILE CA (1907 TO DATE)
12 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
556 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> fiel stnguide
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"HELP COMMANDS" at an arrow prompt (=>).

=> file stnguide

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	40.35	40.56

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=> file hcaplus
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
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FULL ESTIMATED COST                                         0.12      40.68

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FILE COVERS 1907 - 23 Oct 2007  VOL 147 ISS 18
FILE LAST UPDATED: 22 Oct 2007  (20071022/ED)

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 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> s L1-L6

          2385 L1
           925 L2
          2201 L3
          2201 L4
           707 L5
           556 L6
L7        4414 (L1 OR L2 OR L3 OR L4 OR L5 OR L6)

=> s dopamine(2a)d4

         90586 DOPAMINE
         14213 D4
L8        1434 DOPAMINE(2A)D4

=> s l7 and l8

L9          65 L7 AND L8

=> s l9 and (PY<2003 or AY<2003 or PRY<2003)

      22908173 PY<2003
       4465709 AY<2003
       3944515 PRY<2003
L10         24 L9 AND (PY<2003 OR AY<2003 OR PRY<2003)

=> file stnguide

COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         2.60      43.28

FILE 'STNGUIDE' ENTERED AT 14:48:48 ON 23 OCT 2007
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FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Oct 19, 2007 (20071019/UP).

=> d l10 1-24 ti
YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS' - CONTINUE? (Y)/N:y

L10 ANSWER 1 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Stereoisomers of p-hydroxy-milnacipran, and therapeutic use

L10 ANSWER 2 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
TI In vitro and in vivo pharmacological profile of 4-(4-fluorobenzylidene)-1-{2-[5-(4-fluorophenyl)-1H-pyrazol-4-yl]ethyl} piperidine (NRA0161)

L10 ANSWER 3 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Schizophrenia: genesis, receptorology and current therapeutics

L10 ANSWER 4 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Ziprasidone: a novel antipsychotic agent with a unique human receptor binding profile

L10 ANSWER 5 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Dopamine receptor responsivity in schizophrenic patients in a drug-free state and after treatment with olanzapine

L10 ANSWER 6 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Long-term effects of olanzapine, risperidone, and quetiapine on dopamine receptor types in regions of rat brain: implications for antipsychotic drug treatment

L10 ANSWER 7 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Characterization of dopaminergic compounds at hD2short, hD4.2 and hD4.7 receptors in agonist-stimulated [35S]GTPγS binding assays

L10 ANSWER 8 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Nonconserved residues in the second transmembrane-spanning domain of the D4 dopamine receptor are molecular determinants of D4-selective pharmacology

L10 ANSWER 9 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Increase of Dialysate Dopamine in the Bed Nucleus of Stria Terminalis by Clozapine and Related Neuroleptics

L10 ANSWER 10 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
TI The receptor binding profile of cis-flupentixol

L10 ANSWER 11 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
TI In vivo receptor occupancy of NRA0045, a putative atypical antipsychotic, in rats

L10 ANSWER 12 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Expression and characterization of a dopamine D4R variant associated with delusional disorder

L10 ANSWER 13 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Differential regulation of D2 and D4 dopamine receptor mRNAs in the primate cerebral cortex vs. neostriatum: effects of chronic treatment with typical and atypical antipsychotic drugs

L10 ANSWER 14 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Disposition and metabolism of olanzapine in mice, dogs, and rhesus monkeys

L10 ANSWER 15 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
TI [35S]Guanosine-5'-O-(3-thio)triphosphate binding as a measure of efficacy at human recombinant dopamine D4.4 receptors: actions of antiparkinsonian and antipsychotic agents

L10 ANSWER 16 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Disposition and metabolism of olanzapine in mice, dogs, and rhesus monkeys

L10 ANSWER 17 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Alniditan, a new 5-hydroxytryptamine1D agonist and migraine-abortive agent: ligand-binding properties of human 5-hydroxytryptamine1Dα, human 5-hydroxytryptamine1Dβ, and calf 5-hydroxyptryptamineaD receptors investigated with [3H]5-hydroxytryptamine and [3H]alniditan

L10 ANSWER 18 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Iloperidone binding to human and rat dopamine and 5-HT receptors

L10 ANSWER 19 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Effects of typical and atypical antipsychotic drugs on freezing behavior induced by conditioned fear

L10 ANSWER 20 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Preparation of imidazo[1,2-a]pyridines dopamine D4 -receptor antagonist cardiovascular and CNS agents

L10 ANSWER 21 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Radioreceptor binding profile of the atypical antipsychotic olanzapine

L10 ANSWER 22 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
TI D4 dopamine receptor binding affinity does not distinguish between typical and atypical antipsychotic drugs

L10 ANSWER 23 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Does the dopamine receptor subtype selectivity of antipsychotic agents provide useful leads for the development of novel therapeutic agents?

L10 ANSWER 24 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Biphasic displacement of [3H]YM-09151-2 binding in the rat brain by thioridazine, risperidone and clozapine, but not by other antipsychotics

=> d l10 1-24 ti abs bib
YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS' - CONTINUE? (Y)/N:y

L10 ANSWER 1 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Stereoisomers of p-hydroxy-milnacipran, and therapeutic use
AB The invention relates generally to the enantiomers of p-hydroxymilnacipran or congeners thereof. Biol. assays revealed that racemic p-hydroxymilnacipran is approx. equipotent in inhibiting serotonin and norepinephrine uptake (IC50 = 28.6 nM for norepinephrine, IC50 = 21.7 nM for serotonin). Interestingly, (+)-p-hydroxymilnacipran is a more potent inhibitor of norepinephrine uptake than serotonin uptake (IC50 = 10.3 nM for norepinephrine, IC50 = 22 nM for serotonin). In contrast, (-)-p-hydroxymilnacipran is a more potent inhibitor of serotonin uptake compared to norepinephrine uptake (IC50 = 88.5 nM for norepinephrine, IC50 = 40.3 nM for serotonin). The invention also relates to salts and prodrug forms of the above compds. In certain embodiments, the compds. of the invention and a pharmaceutically acceptable excipient are combined to prepare a formulation for administration to a patient. Finally,the invention relates to methods of treating mammals suffering from various afflictions, e.g., depression, chronic pain, or fibromyalgia, comprising

administering to a mammal in need thereof a therapeutically effective amount of a compound of the invention. Compound preparation is included.

AN 2004:392439 HCAPLUS <<LOGINID::20071023>>

DN 140:400095

TI Stereoisomers of p-hydroxy-milnacipran, and therapeutic use

IN Rariy, Roman V.; Heffernan, Michael; Buchwald, Stephen L.; Swager, Timothy M.

PA Collegium Pharmaceutical, Inc., USA

SO PCT Int. Appl., 163 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 6

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004039320	A2	20040513	WO 2003-US33681	20031022 <--
	WO 2004039320	A3	20040624		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
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	AU 2003284342	A1	20040525	AU 2003-284342	20031022 <--
	US 2004142904	A1	20040722	US 2003-691465	20031022 <--
	US 7038085	B2	20060502		
	EP 1578719	A2	20050928	EP 2003-776524	20031022 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	JP 2006503920	T	20060202	JP 2005-501895	20031022 <--
	MX 2005PA04381	A	20060210	MX 2005-PA4381	20050422 <--
	IN 2005CN01003	A	20070824	IN 2005-CN1003	20050524 <--
PRAI	US 2002-421640P	P	20021025 <--		
	US 2002-423062P	P	20021101 <--		
	US 2003-445142P	P	20030205		
	WO 2003-US33681	W	20031022		

OS MARPAT 140:400095

L10 ANSWER 2 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN

TI In vitro and in vivo pharmacological profile of 4-(4-fluorobenzylidene)-1-{2-[5-(4-fluorophenyl)-1H-pyrazol-4-yl]ethyl} piperidine (NRA0161)

AB Atypical antipsychotic properties of 4-(4-fluorobenzylidene)-1-{2-[5-(4-fluorophenyl)-1H-pyrazol-4-yl]ethyl} piperidine (NRA0161) were investigated by in vitro receptor affinities, in vivo receptor occupancies and findings were compared with those of risperidone and haloperidol in rodent behavioral studies. In in vitro receptor binding studies, NRA0161 has a high affinity for human cloned dopamine D4 and 5-HT2A receptor with Ki values of 1.00 and 2.52 nM, resp. NRA0161 had a relatively high affinity for the α1 adrenoceptor (Ki; 10.44 nM) and a low affinity for the dopamine D2 receptor (Ki; 95.80 nM). In in vivo receptor binding studies, NRA0161 highly occupied the 5-HT2A receptor in rat frontal cortex. In contrast, NRA0161 did not occupy the striatal D2 receptor. In behavioral studies, NRA0161, risperidone and haloperidol antagonized the locomotor hyperactivity in mice, as induced by methamphetamine (MAP). At a higher dosage, NRA0161, risperidone and haloperidol dose-dependently antagonized the MAP-induced stereotyped behavior in mice and NRA0161 dose-dependently and significantly induced catalepsy in rats. The ED50 value in inhibiting the MAP-induced locomotor hyperactivity was 30 times lower than that inhibiting the MAP-induced

stereotyped behavior and 50 times lower than that which induced catalepsy. These findings suggest that NRA0161 may have atypical antipsychotic activities yet without producing extrapyramidal side effects.

AN 2002:725209 HCAPLUS <<LOGINID::20071023>>
DN 138:379011
TI In vitro and in vivo pharmacological profile of 4-(4-fluorobenzylidene)-1-{2-[5-(4-fluorophenyl)-1H-pyrazol-4-yl]ethyl} piperidine (NRA0161)
AU Suzuki, Yoshiko; Funakoshi, Takeo; Chaki, Shigeyuki; Kawashima, Naoya; Ogawa, Shin-ichi; Kumagai, Toshihito; Nakazato, Atsurou; Komurasaki, Toshi; Okuyama, Shigeru
CS Molecular Biology Laboratory, Taisho Pharmaceutical Co., Ltd., Saitama-shi, Saitama, 330-8530, Japan
SO Life Sciences (2002), 71(22), 2603-2615
CODEN: LIFSAK; ISSN: 0024-3205
PB Elsevier Science Inc.
DT Journal
LA English
RE.CNT 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 3 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Schizophrenia: genesis, receptorology and current therapeutics
AB A review. Schizophrenia is a debilitating mental disease affecting approx. 1% of the population worldwide. Since the discovery of the first modern treatment for schizophrenia, chlorpromazine, in 1952 there have been many new structures investigated, only a small fraction of which have resulted in clin. useful drugs. Of these, haloperidol may be regarded as the drug for first line treatment. Since then, clozapine has emerged as the benchmark therapeutic ameliorating pos. and neg. symptoms and devoid of movement disorders, with its greatest feature being improvement of treatment-resistant patients. However, a major, potential lethal side-effect of clozapine is the induction of agranulocytosis, a blood disorder with unknown mechanism that results in lowered white-blood cell counts and consequent susceptibility to infections. In the 50 yr of antipsychotic drug development, several novel theories have evolved that focus on receptor sub-types (serotonin 5-HT2A, dopamine D2 and D4) and the degree to which they need to be selectively attenuated by the drugs. Also of significance is the location of these receptors in the brain in relation to the disease state, the myriad of side-effects associated with antipsychotics and physicochem. properties of antipsychotic mols. relative to models of the drugs and the GPCR receptors involved. The techniques for investigation have shown increasing sophistication and refinement over this period, involving cloned receptors and PET scanning for determination of receptor location, d. and binding, and rate consts. at receptors. Knowledge of receptor structure, although in its infancy since no membrane bound CNS-receptor has yet been crystallized, is likely to benefit substantially with advances in computer-aided modeling. Overall, these new techniques have resulted in a number of novel antipsychotics such as risperidone, sertindole, olanzapine, seroquel, zotepine and ziprasidone, whose design, synthesis and testing has benefited enormously from the accumulated knowledge base of the past 50 yr. In this review, we will provide a comprehensive update of the theories of action and clin. profiles of the latest drugs listed. The following appraisal of the literature will provide the practising medicinal chemist interested in this critical area of research with sufficient insight and understanding, to embark on productive investigations into the design and development of new therapeutic agents devoid of clin. limiting side-effects.
AN 2002:275553 HCAPLUS <<LOGINID::20071023>>
DN 137:163110
TI Schizophrenia: genesis, receptorology and current therapeutics
AU Capuano, B.; Crosby, I. T.; Lloyd, E. J.
CS Department of Medicinal Chemistry, Victorian College of Pharmacy, Monash University, Parkville, 3052, Australia
SO Current Medicinal Chemistry (2002), 9(5), 521-548

CODEN: CMCHE7; ISSN: 0929-8673
PB Bentham Science Publishers
DT Journal; General Review
LA English
RE.CNT 286 THERE ARE 286 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 4 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Ziprasidone: a novel antipsychotic agent with a unique human receptor binding profile
AB Ziprasidone is a novel antipsychotic agent with a unique combination of pharmacol. activities at human receptors. Ziprasidone has high affinity for human 5-HT receptors and for human dopamine D2 receptors. Ziprasidone is a 5-HT1A receptor agonist and an antagonist at 5-HT2A, 5-HT2C and 5-HT1B/1D receptors. Addnl., ziprasidone inhibits neuronal uptake of 5-HT and norepinephrine comparable to the antidepressant imipramine. This unique pharmacol. profile of ziprasidone may be related to its clin. effectiveness as a treatment for the pos., neg. and affective symptoms of schizophrenia with a low propensity for extrapyramidal side effects, cognitive deficits and weight gain.
AN 2001:609740 HCAPLUS <<LOGINID::20071023>>
DN 136:477
TI Ziprasidone: a novel antipsychotic agent with a unique human receptor binding profile
AU Schmidt, A. W.; Lebel, L. A.; Howard, H. R.; Zorn, S. H.
CS Groton Laboratories, CNS Discovery, Pfizer Global Research and Development, Groton, CT, 06340-1596, USA
SO European Journal of Pharmacology (2001), 425(3), 197-201
CODEN: EJPHAZ; ISSN: 0014-2999
PB Elsevier Science B.V.
DT Journal
LA English
RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 5 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Dopamine receptor responsivity in schizophrenic patients in a drug-free state and after treatment with olanzapine
AB Olanzapine is a novel atypical antipsychotic with affinity for a number of neurotransmitter receptors including dopamine D1, D2, D4
, serotonin 5HT2A, 5HT2C, histamine H1, a1-adrenergic, and muscarinic receptors. A neuroendocrinol. method to check the degree of dopamine receptor blocking is by measuring the prolactin (PRL) responses to acute (i.m.) administration of haloperidol (HAL). The authors applied this test in a group of male patients with DSM-IV schizophrenia in the drug-free state. The patients were subsequently treated with olanzapine (OLZ) (mean daily dose: 22.5±5.8) and the test was repeated six weeks later. For the HAL-test, 5mg HAL were injected i.m. and blood samples were taken at times 0, 30, 60, 90 and 120 min. Fourteen patients enrolled in the study. Psychopathol. was assessed by means of the Brief Psychiatric Rating Scale (BPRS). Six weeks treatment with OLZ resulted in significant decreases in the total BPRS score and on the score of its subscales for pos., neg., and general psychopathol. Comparison of the PRL response patterns, after HAL administration by anal. of variance for repeated measures (ANOVAR) for drug treatment and time, revealed a highly significant time effect ($F=28.98$, $p=0.000$) and a significant treatment by time interaction ($F=8.27$, $p=0.000008$). Namely, in the drug-free state significant increases were found in the PRL levels after i.m. HAL administration which were significantly reduced during treatment with OLZ, indicating moderate receptor blockade.
AN 2001:350432 HCAPLUS <<LOGINID::20071023>>
DN 135:221172
TI Dopamine receptor responsivity in schizophrenic patients in a drug-free state and after treatment with olanzapine

AU Lykouras, Lefteris; Markianos, Manolis; Hatzimanolis, John; Oulis, Panayotis
CS Athens University Medical School Department of Psychiatry, Schizophrenia Research Program, Eginition Hospital, Athens, 11528, Greece
SO Progress in Neuro-Psychopharmacology & Biological Psychiatry (2001), 25(3), 507-518
CODEN: PNPPD7; ISSN: 0278-5846
PB Elsevier Science Inc.
DT Journal
LA English
RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 6 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Long-term effects of olanzapine, risperidone, and quetiapine on dopamine receptor types in regions of rat brain: implications for antipsychotic drug treatment
AB Changes in members of the dopamine (DA) D1-like (D1, D5) and D2-like (D2, D3, D4) receptor families in rat forebrain regions were compared by quant. in vitro receptor autoradiog. after prolonged treatment (28 days) with the atypical antipsychotics olanzapine, risperidone, and quetiapine. Olanzapine and risperidone, but not quetiapine, significantly increased D2 binding in medial prefrontal cortex (MPC; 67% and 34%), caudate-putamen (CPu; average 42%, 25%), nucleus accumbens (NAc; 37%, 28%), and hippocampus (HIP; 53%, 30%). Olanzapine and risperidone, but not quetiapine, produced even greater up-regulation of D4 receptors in CPu (61%, 37%), NAc (65%, 32%), and HIP (61%, 37%). D1-like and D3 receptors in all regions were unaltered by any treatment, suggesting their minimal role in mediating actions of these antipsychotics. The findings support the hypothesis that antipsychotic effects of olanzapine and risperidone are partly mediated by D2 receptors in MPC, NAc, or HIP, and perhaps D4 receptors in CPu, NAc, or HIP, but not in cerebral cortex. Selective up-regulation of D2 receptors by olanzapine and risperidone in CPu may reflect their ability to induce some extra-pyramidal effects. Inability of quetiapine to alter DA receptors suggests that non-dopaminergic mechanisms contribute to its antipsychotic effects.
AN 2001:321641 HCAPLUS <<LOGINID::20071023>>
DN 135:132309
TI Long-term effects of olanzapine, risperidone, and quetiapine on dopamine receptor types in regions of rat brain: implications for antipsychotic drug treatment
AU Tarazi, Frank I.; Zhang, Kehong; Baldessarini, Ross J.
CS Mailman Research Center, McLean Division of Massachusetts General Hospital, Belmont, MA, USA
SO Journal of Pharmacology and Experimental Therapeutics (2001), 297(2), 711-717
CODEN: JPETAB; ISSN: 0022-3565
PB American Society for Pharmacology and Experimental Therapeutics
DT Journal
LA English
RE.CNT 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 7 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Characterization of dopaminergic compounds at hD2short, hD4.2 and hD4.7 receptors in agonist-stimulated [35S]GTPγS binding assays
AB Dopamine receptor agonists and antagonists have been extensively characterized in radioligand binding assays; only a limited number of labs. have characterized them using a functional assay at multiple receptor subtypes. Expts. were designed to assess four agonists and seven antagonists at three cloned human dopamine receptors using agonist-stimulated [35S]GTPγS binding assays in membranes to quantify the initial cellular event following ligand/receptor interaction. In this model there is constitutive G protein activity

(agonist-independent [35S]GTPγS binding) and potentially constitutive dopamine receptor activity. Thus, discrimination between silent antagonists, partial agonists and inverse agonists is theor. possible. It was anticipated that distinctions could be made regarding efficacy of the seven receptor antagonists to provide insight regarding the therapeutic use of antipsychotic drugs.In membranes prepared from CHO cells transfected to express high densities of human D2short, D4.2 or D4.7 receptors, the dopamine receptor agonists apomorphine, pergolide, quinelorane and quinpirole produced concentration-dependent increases in agonist-stimulated [35S]GTPγS binding. At the hD2short receptor, pergolide and apomorphine were essentially equipotent and more potent than quinelorane and quinpirole; all four agonists displayed similar efficacy at this receptor. At the hD4.2 and the hD4.7 receptors apomorphine was the most potent and pergolide the least efficacious of the four drugs. The ability (both potency and efficacy) of clozapine, haloperidol, olanzapine, quetiapine, risperidone, spiperone and ziprasidone to block apomorphine-stimulated [35S]GTPγS binding and alter basal [35S]GTPγS binding was also assessed. All of the antagonists inhibited apomorphine-stimulated [35S]GTPγS binding with potencies (Kb values) similar to and in rank order consistent with their affinities reported in the literature using radioligand binding assays. Addnl., none of the antagonists altered basal, agonist-independent [35S]GTPγS binding, thus they behaved as pure, silent antagonists at D2short, D4.2 and D4.7 receptors under our conditions. In summary, the data suggest that therapeutic distinctions between typical and atypical antipsychotic drugs cannot be made based on their function at D2short, D4.2 and D4.7 subtypes of dopamine receptors.

AN 2000:295079 HCAPLUS <<LOGINID::20071023>>
DN 133:114944
TI Characterization of dopaminergic compounds at hD2short, hD4.2 and hD4.7 receptors in agonist-stimulated [35S]GTPγS binding assays
AU Gilliland, S. L.; Alper, R. H.
CS Toxicology and Therapeutics, Department of Pharmacology, University of Kansas Medical Center, Kansas City, KS, 66160-7417, USA
SO Naunyn-Schmiedeberg's Archives of Pharmacology (2000), 361(5), 498-504
CODEN: NSAPCC; ISSN: 0028-1298
PB Springer-Verlag
DT Journal
LA English
RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 8 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Nonconserved residues in the second transmembrane-spanning domain of the D4 dopamine receptor are molecular determinants of D4-selective pharmacology
AB The mol. determinants that govern selective ligand binding to the rat D4 dopamine receptor were investigated by substituting D2 dopamine receptor sequences into a D4 dopamine receptor background. The resulting mutant D4 dopamine receptors were then screened with a panel of 10 selective and nonselective ligands, which included two allosteric modulators as sensitive measures of protein conformational changes. Mutation of a phenylalanine at position 88 in the second transmembrane-spanning domain (TMS2) of the D4 receptor to the corresponding valine in the D2 receptor D4-F88V resulted in an .apprx.100-fold decrease in the affinity of the highly D4-selective drug L-750667 without substantially affecting the binding of the other ligands. Mutations at the extracellular side of D4-TMS3 produced moderate decreases in L-750667 binding affinities with concomitant increases in binding affinity for the D2/D3-selective antagonist (-)-raclopride. However, the binding affinities of these same D4-TMS3 mutants for the allosteric modulator isomethylbutylamiloride also were an anomalous 6- to 20-fold higher than either wild-type receptor. In the combined D4-F88V/TMS3

mutants, L-750667 binding affinity was further decreased, but this decrease was not additive. More importantly, the combined D4-F88V/TMS3 mutants had (-)-raclopride and isomethylbutylamiloride binding properties that reverted back to those of the wild-type D4-receptor. In contrast to the D4-F88V mutant, the adjacent D4-L87W mutant had an increased affinity for ligands with extended structures, but had essentially no effect on ligands with compact structures. These findings demonstrate that two residues near the extracellular side of D4-TMS2 are critical mol. determinants for the selective binding of L-750667 and ligands with extended structures.

AN 2000:17474 HCAPLUS <<LOGINID::20071023>>

DN 132:146748

TI Nonconserved residues in the second transmembrane-spanning domain of the D4 dopamine receptor are molecular determinants of D4-selective pharmacology

AU Schetz, John A.; Benjamin, Peter S.; Sibley, David R.

CS Molecular Neuropharmacology Section, Experimental Therapeutics Branch, National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda, MD, USA

SO Molecular Pharmacology (2000), 57(1), 144-152
CODEN: MOPMA3; ISSN: 0026-895X

PB American Society for Pharmacology and Experimental Therapeutics

DT Journal

LA English

RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 9 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN

TI Increase of Dialysate Dopamine in the Bed Nucleus of Stria Terminalis by Clozapine and Related Neuroleptics

AB Neuroleptics are known to stimulate dopamine release in neostriatal terminal areas. In the present study, we have investigated by brain microdialysis in freely moving rats the effect of typical and atypical neuroleptics on dopamine transmission in the bed nucleus of stria terminalis, a dopamine terminal area belonging to the limbic system and recently assigned the so-called extended amygdala. Mean basal dialyzate dopamine values were 14.3 f moles/20 μl sample. Dopamine output in dialyzates was increased dose-dependently by clozapine (maximum +158%, 298%, and 461% of basal at 5, 10, and 20 mg/kg IP, resp.), risperidone (maximum +115% and 221% of basal at 1 and 3 mg/kg IP, resp.), olanzapine (maximum +138% and 235% of basal at 3 and 6 mg/kg IP, resp.), BIMG 80 (maximum +64% and 164% of basal at 3 and 5 mg/kg IP, resp.), amperozide (maximum +110% and 194% of basal at 3 and 6 mg/kg IP, resp.). The selective dopamine D4 antagonist L-745,870 increased dialyzate dopamine but at rather high doses and not as effectively as clozapine (maximum +32%, 89%, and 130% of basal at 2.7, 5.4, and 10.8 mg/kg IP, resp.). The typical neuroleptic haloperidol (0.1 and 0.5 mg/kg SC) and the selective D2 antagonist raclopride (0.14, 0.56, and 2.1 mg/kg SC), the serotonergic 5-HT2 antagonist ritanserin (0.5 and 1.5 mg/kg IP), and the adrenergic α1 antagonist prazosin (0.91 and 2.73 mg/kg IP) did not affect dialyzate dopamine in the bed nucleus of stria terminalis. Saline (1 mL/kg SC or 3 mL/kg IP) did not modify dialyzate dopamine. Therefore, atypical neuroleptics share the ability of stimulating dopamine transmission in the bed nucleus of stria terminalis, but this property is not mimicked by any of the drug tested that selectively act on individual receptors among those that are affected by atypical neuroleptics. These observations raise the possibility that the property of increasing dopamine transmission in the bed nucleus of stria terminalis is the result of combined blockade of dopamine, serotonin, and noradrenaline receptors and that might be predictive of an atypical neuroleptic profile.

AN 2000:10312 HCAPLUS <<LOGINID::20071023>>

DN 133:572

TI Increase of Dialysate Dopamine in the Bed Nucleus of Stria Terminalis by Clozapine and Related Neuroleptics

AU Carboni, E.; Rolando, M. T. P.; Silvagni, A.; Di Chiara, G.
CS C.N.R. Center for Neuropharmacology, Department of Toxicology, University of Cagliari, Cagliari, Italy
SO Neuropsychopharmacology (1999), Volume Date 2000, 22(2), 140-147
CODEN: NEROEW; ISSN: 0893-133X
PB Elsevier Science Inc.
DT Journal
LA English
RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 10 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
TI The receptor binding profile of cis-flupentixol
AB The action profile was investigated of flupentixol on different neurotransmitter receptors in comparison with other neuroleptics. Its binding was studied to the dopamine receptor subtypes D1, D2S, D3, and D4-4 together with serotonin 5-HT2A-, 5HT2C-, and α-adrenergic receptors. Cis-flupentixol differed from haloperidol. It showed similarities with atypical neuroleptics especially in its interaction with 5-HT2A- (and 5HT2C-) receptors and high affinity to dopamine-D1 receptors. The authors suggest its classification as atypical rather than typical (=classical) neuroleptic.
AN 2000:249 HCAPLUS <<LOGINID::20071023>>
DN 132:44885
TI The receptor binding profile of cis-flupentixol
AU Glaser, T.; Sommermeyer, H.; Fassbender, M.; Mauler, F.
CS Germany
SO Flupentixol - Typisches oder Atypisches Wirkspektrum? : Pharmakologie, Antipsychotische Wirkung, neue Indikationen (1998), 9-21.
Editor(s): Glaser, T.; Soyka, M. Publisher: Dr. Dietrich Steinkopff Verlag GmbH & Co. KG, Darmstadt, Germany.
CODEN: 68MEAY
DT Conference
LA German
RE.CNT 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 11 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
TI In vivo receptor occupancy of NRA0045, a putative atypical antipsychotic, in rats
AB We have previously reported that (R)-(+)-2-amino-4-(4-fluorophenyl)-5-[1-[4-(4-fluorophenyl)-4-oxobut yl]pyrrolidin-3-yl]thiazole (NRA0045) is a novel antipsychotic agent with affinities for dopamine D4, 5-hydroxytryptamine 2A (5-HT2A) and α1 receptors. In the present study, in vivo receptor occupancy of 5-HT2A, α1, dopamine D2 and D3 receptors by NRA0045 was assessed, based on in vivo and ex vivo receptor binding, and findings were compared to reference antipsychotic drugs (haloperidol, risperidone, clozapine). I.p. administration of haloperidol highly occupied the dopamine D2 receptor in the striatum and nucleus accumbens, and α1 adrenoceptors in the frontal cortex. Occupation of the 5-HT2A receptor in the frontal cortex and the dopamine D3 receptor in the nucleus accumbens and islands of Calleja was moderate. By contrast, atypical antipsychotics such as risperidone and clozapine dose-dependently occupied the 5-HT2A receptor in the frontal cortex, with moderate to negligible occupancy of the D2 receptor in the striatum and the nucleus accumbens. Clozapine and risperidone also occupied the α1 adrenoceptor in the frontal cortex, and clozapine did not occupy the dopamine D3 receptor. As seen with other atypical antipsychotics, i.p. administration of NRA0045 dose-dependently occupied the 5-HT2A receptor and the α1 adrenoceptor in the frontal cortex, while it was without effect on dopamine D2 and D3 receptors in the striatum, nucleus accumbens and islands of Calleja. Thus, the strong occupancy of 5-HT2A and α1 receptors is involved in the pharmacol. action of NRA0045.
AN 1999:504310 HCAPLUS <<LOGINID::20071023>>

DN 131:252464
TI In vivo receptor occupancy of NRA0045, a putative atypical antipsychotic, in rats
AU Chaki, Shigeyuki; Funakoshi, Takeo; Yoshikawa, Ryoko; Okuyama, Shigeru; Kumagai, Toshihito; Nakazato, Atsuro; Nagamine, Masashi; Tomisawa, Kazuyuki
CS 1st Laboratory, Medicinal Research Laboratories, Taisho Pharmaceutical Co. Ltd., Saitama, 330-8530, Japan
SO Neuropharmacology (1999), 38(8), 1185-1194
CODEN: NEPHBW; ISSN: 0028-3908
PB Elsevier Science Ltd.
DT Journal
LA English
RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 12 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Expression and characterization of a dopamine D4R variant associated with delusional disorder
AB Multiple genetic polymorphisms of the human dopamine D4 receptor (hD4R) have been identified including a 12 bp repeat in exon 1 associated with a psychotic condition called delusional disorder. Competition binding assays revealed minor pharmacol. differences between the recombinant A1 (normal) and A2 (delusional) proteins with respect to quinpirole and the antipsychotic clozapine, however no functional differences were detected for receptor activation by dopamine, epinephrine, or norepinephrine. The results suggest that this polymorphism may only confer susceptibility to delusional disorder in combination with other genetic or environmental factors.
AN 1998:72960 HCAPLUS <<LOGINID::20071023>>
DN 128:191185
TI Expression and characterization of a dopamine D4R variant associated with delusional disorder
AU Zenner, Marie-Therese; Nobile, Maria; Henningsen, Robert; Smeraldi, Enrico; Civelli, Olivier; Hartman, Deborah S.; Catalano, Marco
CS Preclinical Neuroscience, Hoffmann-La Roche, Pharmaceutical Research, Basel, 4070, Switz.
SO FEBS Letters (1998), 422(2), 146-150
CODEN: FEBLAL; ISSN: 0014-5793
PB Elsevier Science B.V.
DT Journal
LA English
RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 13 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Differential regulation of D2 and D4 dopamine receptor mRNAs in the primate cerebral cortex vs. neostriatum: effects of chronic treatment with typical and atypical antipsychotic drugs
AB The RNase Protection Assay was used to examine the regulation of D2 and D4 dopamine receptor mRNAs in the cerebral cortex and neostriatum of nonhuman primates after chronic treatment with a wide spectrum of antipsychotic medications (chlorpromazine, clozapine, haloperidol, molindone, olanzapine, pimozide, remoxipride and risperidone). Tiapride, a D2 antagonist that lacks antipsychotic activity, was also included. All drugs were administered orally for 6 mo at doses recommended for humans. All antipsychotic drug treatments examined in this study caused a statistically significant up-regulation of both the long and short isoforms of the D2 receptor mRNAs in the prefrontal and temporal cortex. Tiapride, in contrast, significantly up-regulated only the level of D2-long mRNA in these areas. The same drug treatments produced less uniform effects in the neostriatum than in the cortex: clozapine and olanzapine failed to significantly elevate either D2-long or D2-short receptor messages in this structure unlike all other drugs,

including tiapride. In both the cerebral cortex and striatum, D4 receptor mRNA was upregulated by certain typical (chlorpromazine and haloperidol) and certain atypical (clozapine, olanzapine and risperidone) antipsychotic agents as well as by tiapride. Other drugs of the typical (molindone and pimozide) and atypical (remoxipride) classes had no effect on D4 mRNA levels in either cortical or striatal tissue. The finding that up-regulation of D2 dopamine receptor mRNAs was a consistently observed effect of a wide range of antipsychotic agents in the cerebral cortex but not in the neostriatum, coupled with the fact that the D2-short isoforms in the cortex were not regulated by a non-antipsychotic D2 antagonist, tiapride, draws attention to the importance of the D2 dopamine receptor in the cerebral cortex as a potentially critical, common site of action of antipsychotic medications.

AN 1997:749549 HCAPLUS <<LOGINID::20071023>>
DN 128:70682
TI Differential regulation of D2 and D4 dopamine receptor mRNAs in the primate cerebral cortex vs. neostriatum: effects of chronic treatment with typical and atypical antipsychotic drugs
AU Lidow, Michael S.; Goldman-Rakic, Patricia S.
CS Section of Neurobiology, Yale University School of Medicine, New Haven, CT, USA
SO Journal of Pharmacology and Experimental Therapeutics (1997), 283(2), 939-946
CODEN: JPETAB; ISSN: 0022-3565
PB Williams & Wilkins
DT Journal
LA English
RE.CNT 66 THERE ARE 66 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 14 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Disposition and metabolism of olanzapine in mice, dogs, and rhesus monkeys
AB Olanzapine (OLZ) is a novel antipsychotic agent with a high affinity for serotonin (5-HT2), dopamine (D1/D2/D4), muscarinic (m1-m5), adrenergic (α1), and histamine (H1) receptors. The pharmacokinetics, excretion, and metabolism of OLZ were studied in CD-1 mice, beagles dogs, and rhesus monkeys after a single oral and/or i.v. dose of [14C]OLZ. After oral administration, OLZ was well absorbed in dogs (absolute bioavailability of 73%) and to the extent of at least 55% in monkeys and 32% in mice. The terminal elimination half-life of OLZ was relatively short in mice and monkeys, (-3 h) and long in dogs (-9 h). In mice and dogs, radioactivity was predominantly eliminated in feces; but, in monkeys, the major route of elimination of radioactivity was urine. Dogs and monkeys excreted in urine, resp., 38% and 55% of the dose over a 168-h period, whereas the fraction of the dose excreted in urine of mice over the collection period (120 h) was 32%. OLZ was subject to substantial first-pass metabolism; at the tmax, OLZ accounted for 19%, 18% and 18% of the radioactivity in mice, dogs, and monkeys, resp. The ratio of AUC OLZ to AUC radioactivity was resp., 10%, 14%, and 4% in mice, dogs, and monkeys. The principal urinary metabolites in mice were 7-hydroxy OLZ glucuronide, 2-hydroxymethyl OLZ, and 2-carboxy OLZ accounting for .apprx.10%, 4%, and 2% of the dose. Metabolites that were present in urine in lesser amts. were 7-hydroxy OLZ, N-desmethyl OLZ, and N-desmethyl-2-hydroxymethyl OLZ. In dogs, the major metabolite accounting for 8% of the dose was 7-hydroxy-N-oxide OLZ. Other metabolites identified were 2-hydroxymethyl OLZ, 2-carboxy OLZ, N-oxide OLZ, 7-hydroxy OLZ, and its glucuronide and N-desmethyl OLZ. The major metabolite in monkey urine was N-desmethyl-2-carboxy OLZ, and accounted for .apprx.17% of the dose. In addition, N-oxide-2-hydroxymethyl OLZ, N-oxide-2-carboxy OLZ, N-desmethyl-2-hydroxymethyl, 2-carboxy OLZ, and 2-hydroxymethyl OLZ were identified in monkeys urine. Thus, in mice and dogs, OLZ was metabolized through aromatic hydroxylation, allylic oxidation, N-dealkylation, and N-oxidation reactions. In monkeys, OLZ was biotransformed mainly through double

oxidation reactions involving the allylic carbon and Me piperazine nitrogen. Whereas the oxidative metabolic profile of OLZ in animals was similar to that of humans, animals were notable for not forming appreciable amts. of the principal human metabolite (i.e. 10-N-glucuronide OLZ).

AN 1997:634273 HCAPLUS <<LOGINID::20071023>>
Correction of: 1997:329809

DN 127:215146
Correction of: 127:60154

TI Disposition and metabolism of olanzapine in mice, dogs, and rhesus monkeys

AU Mattiuz, Edward; Franklin, Ronald; Gillespie, Todd; Murphy, Anthony; Bernstein, John; Chiu, Andre; Hotten, Terry; Kassahun, Kelem

CS Dep. Drug Metabolism, Lilly Corp. Cent., Eli Lilly Co., Indianapolis, IN, 46285, USA

SO Drug Metabolism and Disposition (1997), 25(5), 573-583
CODEN: DMDSAI; ISSN: 0090-9556

PB Williams & Wilkins

DT Journal

LA English

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 15 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN

TI [35S]Guanosine-5'-O-(3-thio)triphosphate binding as a measure of efficacy at human recombinant dopamine D4.4 receptors: actions of antiparkinsonian and antipsychotic agents

AB Recombinant human dopamine D4.4 receptor-mediated G protein activation was characterized in membranes of transfected mammalian (Chinese hamster ovary) cells by the use of [35S]guanosine-5'-O-(3-thio)triphosphate ([35S]GTPγS) binding. An initial series of expts. defined the conditions (3 μM GDP, 100 mM NaCl, 3 mM MgCl2) under which optimal stimulation (2.2-fold increase in specific [35S]GTPγS binding) was achieved with the endogenous agonist dopamine. The number of dopamine-activated G proteins in Chinese hamster ovary-D4.4 membranes was determined through [35S]GTPγS isotopic dilution saturation binding, yielding a Bmax value of 2.29 pmol/mg. This compared with a D4.4 receptor Bmax value of 1.40 pmol/mg determined by [3H]spiperone saturation binding, indicating that 1 or 2 G proteins were activated per D4.4 receptor and that there were few or no "spare receptors" in this cell line. Under these conditions, the efficacy for stimulation of [35S]GTPγS binding at D4.4 receptors of 12 dopaminergic agonists was determined Several antiparkinsonian drugs, including ropinirole, quinerolane and lisuride, exhibited agonist activity at D4.4 receptors (Emax = 74.3%, 72.4% and 32.2%, resp., compared with dopamine = 100%). The EC50 values for agonist stimulation of [35S]GTPγS binding correlated well with the inhibition consts. derived from competition binding with [3H]spiperone (r = +.99). However, other antiparkinsonian drugs (bromocriptine, L-DOPA and terguride) showed low affinity and/or were devoid of agonist activity at D4.4 receptors. The potency at D4.4 receptors of the novel, selective D4.4 receptor antagonist L 745,870 was determined, indicting that it has high affinity (Ki = 1.99 nM) without detectable agonist activity. Furthermore, L 745,870 completely inhibited dopamine-stimulated [35S]GTPγS binding with a Kb value of 1.07 nM. The action of an addnl. 20 chemical diverse dopaminergic ligands, including clozapine, ziprasidone, sertindole, olanzapine and several other "atypical" antipsychotics, in advanced development was investigated. Each of these ligands shifted the dopamine stimulation curve to the right in a parallel manner consistent with competitive antagonism at this site and yielding Kb values (32.6, 22.4, 17.2 and 26.5 nM, resp.) that agreed closely with their Ki values (38.0, 14.9, 18.5 and 26.1 nM). In contrast, raclopride and seroquel exhibited low affinity at D4.4 receptors (Ki > 1000 nM). Other compds. that showed antagonist activity at D4.4 receptors included the 5-hydroxytryptamine2A receptor antagonist fananserin (RP 62203), the sigma ligand BMY 14,802 and the D3 receptor antagonist GR 103,691. In conclusion, dopamine

D4.4 receptor activity is unlikely to be an important factor in the clin. effectiveness of antiparkinsonian drugs, although low agonist efficacy at D4.4 receptors might be associated with a lesser incidence of side effects. Furthermore, antagonist activity at D4.4 receptors is a common property of many typical and atypical antipsychotic agents.

AN 1997:457442 HCAPLUS <<LOGINID::20071023>>
DN 127:171462
TI [35S]Guanosine-5'-O-(3-thio)triphosphate binding as a measure of efficacy at human recombinant dopamine D4.4 receptors: actions of antiparkinsonian and antipsychotic agents
AU Newman-Tancredi, A.; Audinot, V.; Chaput, C.; Verriele, L.; Millan, M. J.
CS Dep. of Psychopharmacology, Institut de Recherches Servier, Croissy-sur-Seine, 78290, Fr.
SO Journal of Pharmacology and Experimental Therapeutics (1997), 282(1), 181-191
CODEN: JPETAB; ISSN: 0022-3565
PB Williams & Wilkins
DT Journal
LA English

L10 ANSWER 16 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Disposition and metabolism of olanzapine in mice, dogs, and rhesus monkeys
AB Olanzapine (OLZ) is a novel antipsychotic agent with a high affinity for serotonin (5-HT2), dopamine (D1/D2/D4), muscarinic (m1-m5), adrenergic (α1), and histamine (H1) receptors. The pharmacokinetics, excretion, and metabolism of OLZ were studied in CD-1 mice, beagles dogs, and rhesus monkeys after a single oral and/or i.v. dose of [14C]OLZ. After oral administration, OLZ was well absorbed in dogs (absolute bioavailability of 73%) and to the extent of at least 55% in monkeys and 32% in mice. The terminal elimination half-life of OLZ was relatively short in mice and monkeys, (.apprx.3 h) and long in dogs (.apprx.9 h). In mice and dogs, radioactivity was predominantly eliminated in feces; but, in monkeys, the major route of elimination of radioactivity was urine. Dogs and monkeys excreted in urine, resp., 38% and 55% of the dose over a 168-h period, whereas the fraction of the dose excreted in urine of mice over the collection period (120 h) was 32%. OLZ was subject to substantial first-pass metabolism; at the tmax, OLZ accounted for 19%, 18% and 18% of the radioactivity in mice, dogs, and monkeys, resp. The ratio of AUC OLZ to AUC radioactivity was, resp., 10%, 14%, and 4% in mice, dogs, and monkeys. The principal urinary metabolites in mice were 7-hydroxy OLZ glucuronide, 2-hydroxymethyl OLZ, and 2-carboxy OLZ accounting for .apprx.10%, 4%, and 2% of the dose. Metabolites that were present in urine in lesser amts. were 7-hydroxy OLZ, N-desmethyl OLZ, and N-desmethyl-2-hydroxymethyl OLZ. In dogs, the major metabolite accounting for .apprx.8% of the dose was 7-hydroxy-N-oxide OLZ. Other metabolites identified were 2-hydroxymethyl OLZ, 2-carboxy OLZ, N-oxide OLZ, 7-hydroxy OLZ, and its glucuronide and N-desmethyl OLZ. The major metabolite in monkey urine was N-desmethyl-2-carboxy OLZ, and accounted for .apprx.17% of the dose. In addition, N-oxide-2-hydroxymethyl OLZ, N-oxide-2-carboxy OLZ, N-desmethyl-2-hydroxymethyl, 2-carboxy OLZ, and 2-hydroxymethyl OLZ were identified in monkeys urine. Thus, in mice and dogs, OLZ was metabolized through aromatic hydroxylation, allylic oxidation, N-dealkylation, and N-oxidation reactions. In monkeys, OLZ was biotransformed mainly through double oxidation reactions involving the allylic carbon and Me piperazine nitrogen. Whereas the oxidative metabolic profile of OLZ in animals was similar to that of humans, animals were notable for not forming appreciable amts. of the principal human metabolite (i.e. 10-N-glucuronide OLZ).

AN 1997:329809 HCAPLUS <<LOGINID::20071023>>
DN 127:60154
TI Disposition and metabolism of olanzapine in mice, dogs, and rhesus monkeys
AU Mattiuz, Edward; Franklin, Ronald; Gillespie, Todd; Murphy, Anthony; Bernstein, John; Chiur, Andre; Hotten, Terry; Kassahun, Kelem
CS Dep. Drug Metabolism, Lilly Corporate Center, Eli Lilly Company,

Indianapolis, IN, 46285, USA
SO Drug Metabolism and Disposition (1997), 25(5), 573-583
CODEN: DMDSAI; ISSN: 0090-9556
PB Williams & Wilkins
DT Journal
LA English
RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 17 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Alniditan, a new 5-hydroxytryptamine1D agonist and migraine-abortive agent: ligand-binding properties of human 5-hydroxytryptamine1Dα, human 5-hydroxytryptamine1Dβ, and calf 5-hydroxyptryptamineaD receptors investigated with [3H]5-hydroxytryptamine and [3H]alniditan
AB Alniditan is a new migraine-abortive agent. It is a benzopyran derivative and therefore structurally unrelated to sumatriptan and other indole-derivs. and to ergoline derivs. The action of sumatriptan is thought to be mediated by 5-hydroxytryptamine (5-HT)1D-type receptors. We investigated the receptor-binding profile in vitro of alniditan compared with sumatriptan and dihydroergotamine for 28 neurotransmitter receptor subtypes, several receptors for peptides and lipid-derived factors, ion channel-binding sites, and monoamine transporters. Alniditan revealed nanomolar affinity for calf substantia nigra 5-HT1D and for cloned h5-HT1Dα, h-HT1Dβ, and h5-HT1A receptors (Ki = 0.8, 0.4, 1.1, and 3.8 nM, resp.). Alniditan was more potent than sumatriptan at 5-HT1D-type and 5-HT1A receptors. Alniditan showed moderate-to-low or no affinity for other investigated receptors; sumatriptan showed addnl. binding to 5-HT1F receptors. Dihydroergotamine had a much broader profile with high affinity for several 5-HT, adrenergic and dopaminergic receptors in signal transduction assays using cells expressing recombinant h5-HT1Dα, h5-HT1Dβ, or h5-HT1A receptors, alniditan (like 5-HT) was a full agonist for inhibition of stimulated adenylyl cyclase (IC50 = 1.1, 1.3, and 74 nM, resp., for alniditan). Therefore, in functional assays, the potency of alniditan was much higher at 5-HT1D receptors than at 5-HT1A receptors. We further compared the properties of [3H]alniditan, as a new radioligand for 5-HT1D-type receptors, with those of [3H]5-HT in membrane prepns. of calf substantia nigra, C6 glioma cells expressing h5-HT1Dα, and L929 cells expressing h5-HT1Dβ receptors. [3H]Alniditan revealed very rapid association and dissociation binding kinetics and showed slightly higher affinity (Kd = 1-2 nM) than [3H]5-HT. We investigated 25 compds. for inhibition of [3H]alniditan and [3H]5-HT binding in the three membrane prepns.; Ki values of the radioligands were largely similar, although some subtle differences appeared. Most compds. did not differentiate between 5-HT1Dα and 5-HT1Dβ receptors, except methylsergide, ritanserin, ocaperidone, risperidone, and ketanserin, which showed 10-60-fold higher affinity for the 5-HT1Dα receptor. The Ki values of the compds. obtained with 5-HT1D receptors in calf substantia nigra indicated that these receptors are of the 5-HT1Dβ-type. We demonstrated that alniditan is a potent agonist at h5-HT1Dα and h5-HT1Dβ receptors; its properties probably underlie its cranial vasoconstrictive and antimigraine properties.
AN 1997:7381 HCAPLUS <<LOGINID::20071023>>
DN 126:99256
TI Alniditan, a new 5-hydroxytryptamine1D agonist and migraine-abortive agent: ligand-binding properties of human 5-hydroxytryptamine1Dα, human 5-hydroxytryptamine1Dβ, and calf 5-hydroxyptryptamineaD receptors investigated with [3H]5-hydroxytryptamine and [3H]alniditan
AU Leysen, Jose E.; Gommeren, Walter; Heylen, Lieve; Luyten, Walter H. M. L.; van de Weyer, Inez; Vanhoenacker, Peter; Haegeman, Guy; Schotte, Alain; van Gompel, Paul; Wouters, Ria; Lesage, Anne S.
CS Dep. Biochemical Pharmacology, Janssen Res. Foundation, Beerse, B-2340, Belg.
SO Molecular Pharmacology (1996), 50(6), 1567-1580
CODEN: MOPMA3; ISSN: 0026-895X

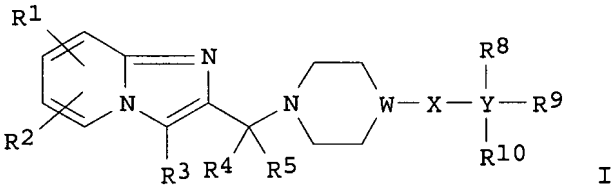
PB Williams & Wilkins
DT Journal
LA English

L10 ANSWER 18 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Iloperidone binding to human and rat dopamine and 5-HT receptors
AB Iloperidone (HP 873; 1-[4-[3-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl]propoxy]-3-methoxyphenyl]ethanone) is a compound currently in clin. trials for the treatment of schizophrenia. Iloperidone displays affinity for dopamine D2 receptors and for 5-HT2A receptors and has a variety of in vivo activities suggestive of an atypical antipsychotic. Here we present an examination of the affinity of iloperidone to a variety of human and rat homologs of dopamine and 5-HT receptor subtypes. We employed receptor binding assays using membranes from cells stably expressing human dopamine D1, D2S, D2L, D3, D4 and D5 and 5-HT2A and 5-HT2C receptors and rat 5-HT6 and 5-HT7 receptors. Iloperidone displayed higher affinity for the dopamine D3 receptor (Ki = 7.1 nM) than for the dopamine D4 receptor (Ki = 25 nM). Iloperidone displayed high affinity for the 5-HT6 and 5-HT7 receptors (Ki = 42.7 and 21.6 nM, resp.), and was found to have higher affinity for the 5-HT2A (Ki = 5.6 nM) than for the 5-HT2C receptor (Ki = 42.8 nM). The potential implications of this receptor binding profile are discussed in comparison with data for other antipsychotic compds.
AN 1996:750480 HCAPLUS <<LOGINID::20071023>>
DN 126:70003
TI Iloperidone binding to human and rat dopamine and 5-HT receptors
AU Kongsamut, Sathapana; Roehr, Joachim E.; Cai, Jidong; Hartman, Harold B.; Weissensee, Paul; Kerman, Lisa L.; Tang, Lei; Sandrasagra, Anthony
CS Neuroscience Research, Hoechst Marion Roussel, Inc., Route 202-206, P.O. Box 6800, Bridgewater, NJ, 08807-0800, USA
SO European Journal of Pharmacology (1996), 317(2/3), 417-423
CODEN: EJPHAZ; ISSN: 0014-2999
PB Elsevier
DT Journal
LA English

L10 ANSWER 19 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Effects of typical and atypical antipsychotic drugs on freezing behavior induced by conditioned fear
AB Atypical antipsychotic drugs (atypical APDs), such as clozapine, ORG 5222, and olanzapine, have been suggested to possess anxiolytic activity in the conflict test and elevated plus-maze test, while several studies have suggested that typical APDs are not anxiolytic in several models of anxiety. The effects of typical and atypical APDs on the acquisition and expression of conditioned fear-induced freezing were investigated. The drugs were administered s.c. to male Sprague-Dawley rats 30 min before foot-shock stress. Twenty-four hours after foot shock, freezing behavior of rats was observed in the shock chamber without shocks. The atypical APD clozapine (0.3-10 mg/kg) dose-dependently inhibited the acquisition of conditioned freezing. Candidates for atypical APDs, ORG 5222 (0.1-1 mg/kg), olanzapine (1-10 mg/kg), and raclopride (3-30 mg/kg), also dose-dependently reduced the acquisition of conditioned freezing. The typical APDs haloperidol (3 mg/kg), spiperone (0.1-1 mg/kg) and nemonapride (1 mg/kg) inhibited the acquisition of conditioned freezing, but their effects were reduced at higher doses. Chlorpromazine, a typical APD, produced about 50% inhibition of the acquisition of conditioned freezing only at the dose of 10 mg/kg. The ED50 values (mg/kg) for inhibiting the acquisition of conditioned freezing was correlated with the Ki values for D4 dopaminergic receptors, but not with the ki values for other monoamine and acetylcholine receptors. On the other hand, clozapine or haloperidol did not change the expression of conditioned freezing. The protective effects of clozapine and other antipsychotic drugs on the acquisition of conditioned freezing may be mediated by blockade of D4 receptors.

AN 1996:734646 HCAPLUS <<LOGINID::20071023>>
DN 126:14642
TI Effects of typical and atypical antipsychotic drugs on freezing behavior induced by conditioned fear
AU Inoue, Takeshi; Tsuchiya, Kiyoshi; Koyama, Tsukasa
CS Dep. of Phychiatry, Hokkaido Univ. Sch. of Medicine, Sapporo, 060, Japan
SO Pharmacology, Biochemistry and Behavior (1996), 55(2), 195-201
CODEN: PBBHAU; ISSN: 0091-3057
PB Elsevier
DT Journal
LA English

L10 ANSWER 20 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Preparation of imidazo[1,2-a]pyridines dopamine D4 -receptor antagonist cardiovascular and CNS agents
GI



I

AB The title compds. [I; R1, R2 = H, halogen, alkyl, cycloalkyl, CN, (un)substituted CONH2, etc.; R3 = H, halogen, CN, OH, alkyl, CHO, etc.; R4-R7 = H, alkyl, cycloalkyl, cycloalkyl, (un)substituted aryl, etc.; R8-R10 = H, halogen, alkyl, cycloalkyl, CN, (un)substituted CONH2, (un)substituted NH2, etc.; W = N, CH; X = direct bond, NR4; Y = Ph, 2-, 3-, 4-pyridyl, pyrimidinyl, pyrazinyl, etc.] [e.g., 6-chloro-2-[[4-(4-methoxyphenyl)-1-piperazinyl]methyl]imidazo[1,2-a]pyridine; m.p. 111-112°], which are dopamine D4-receptor antagonists (e.g., I demonstrate a ki for displacement of 3H-spiperone from human dopamine D4 receptors of <2.5 μM), useful as antipsychotic (no data) and cardiovascular (no data) agents, are prepared
AN 1996:628533 HCAPLUS <<LOGINID::20071023>>
DN 125:275875
TI Preparation of imidazo[1,2-a]pyridines dopamine D4 -receptor antagonist cardiovascular and CNS agents
IN Tenbrink, Ruth E.
PA Pharmacia and Upjohn Company, USA
SO PCT Int. Appl., 88 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9625414	A1	19960822	WO 1996-US1114	19960212 <--
	W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD				
	AU 9648595	A	19960904	AU 1996-48595	19960212 <--
	EP 809642	A1	19971203	EP 1996-904507	19960212 <--

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV

JP 11500123 T 19990106 JP 1996-524966 19960212 <--
US 5912246 A 19990615 US 1997-894179 19970814 <--
US 6013654 A 19990111 US 1998-222560 19981230 <--
PRAI US 1995-388682 A2 19950215 <--
WO 1996-US1114 W 19960212 <--
US 1997-894179 A3 19970814 <--
OS MARPAT 125:275875

L10 ANSWER 21 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Radioreceptor binding profile of the atypical antipsychotic olanzapine
AB The affinities of olanzapine, clozapine, haloperidol, and four potential antipsychotics were compared on binding to the neuronal receptors of a number of neurotransmitters. In both rat tissues and cell lines transfected with human receptors olanzapine had high affinity for dopamine D1, D2, D4, serotonin (5HT)2A, 5HT2C, 5HT3, α1-adrenergic, histamine H1, and five muscarinic receptor subtypes. Olanzapine had lower affinity for α2-adrenergic receptors and relatively low affinity for 5HT1 subtypes, GABAA, β-adrenergic receptors, and benzodiazepine binding sites. The receptor binding affinities for olanzapine was quite similar in tissues from rat and human brain. The binding profile of olanzapine was comparable to the atypical antipsychotic clozapine, while the binding profiles for haloperidol, risperidone, remoxipride, Org 5222, and seroquel were substantially different from that of clozapine. The receptor binding profile of olanzapine is consistent with the antidopaminergic, antiserotonergic, and antimuscarinic activity observed in animal models and predicts atypical antipsychotic activity in man.
AN 1996:138439 HCAPLUS <<LOGINID::20071023>>
DN 124:250583
TI Radioreceptor binding profile of the atypical antipsychotic olanzapine
AU Bymaster, Frank P.; Calligaro, David O.; Falcone, Julie F.; Marsh, Richard D.; Moore, Nicholas A.; Tye, Nicholas C.; Seeman, Philip; Wong, David T.
CS Lilly Research Laboratories, Lilly Corporate Center, Indianapolis, IN, 46285, USA
SO Neuropsychopharmacology (1996), 14(2), 87-96
CODEN: NEROEW; ISSN: 0893-133X
PB Elsevier
DT Journal
LA English

L10 ANSWER 22 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
TI D4 dopamine receptor binding affinity does not distinguish between typical and atypical antipsychotic drugs
AB The affinities of 13 atypical and 12 typical antipsychotic drugs for the cloned rat D4 dopamine receptor and the D4/D2 ratios were examined Of the atypical antipsychotic drugs tested, only clozapine, risperidone, olanzapine, zotepine and tiospirone had affinities less than 20 nM. In fact, many atypical antipsychotic drugs had relatively low affinities for the cloned rat D4 receptor, with Ki values greater than 100 nM (Seroquel, fluperlapine, tenilapine, FG5803 and melperone). Addnl., several typical antipsychotic drugs had high affinities for the cloned rat D4 receptor, with Kis less than 20 nM (loxapine, chlorpromazine, fluphenazine, mesoridazine, thioridazine and trifluoroperazine). The ratios of D2/D4 affinities did not differentiate between these two types of antipsychotic drugs. Thus, D4 dopamine receptor affinity, used as a single measure, does not distinguish between the group of typical and atypical antipsychotic drugs analyzed.
AN 1995:809376 HCAPLUS <<LOGINID::20071023>>
DN 123:246661
TI D4 dopamine receptor binding affinity does not distinguish between typical and atypical antipsychotic drugs
AU Roth, B. L.; Tandra, S.; Burgess, L. H.; Sibley, D. R.; Meltzer, H. Y.
CS Sch. Med., Case Western Reserve Univ., Cleveland, OH, 44106-4935, USA

SO Psychopharmacology (Berlin) (1995), 120(3), 365-8
CODEN: PSCHDL; ISSN: 0033-3158
PB Springer
DT Journal
LA English

L10 ANSWER 23 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Does the dopamine receptor subtype selectivity of antipsychotic agents provide useful leads for the development of novel therapeutic agents?
AB Antipsychotic agents share the ability to antagonize dopamine (DA) receptors, and correlation studies have indicated that the clin. efficacy of neuroleptic agents may be coupled to their affinity for D2 receptors. More recently, a family of DA D2-like receptors has been identified. These receptors include the D2A, D2B, D3 and D4 receptors. On the basis of in vitro receptor-binding studies, it has been suggested that the atypical profile of clozapine might be related to a selective effect on the D4 receptor subtype. We have studied the receptor-binding profiles of a series of antipsychotic agents and evaluated some of the compds. in behavioral assays in the rat. Most of the antipsychotic agents lack selectivity for DA-receptors as well as selectivity for the various DA-receptor subtypes. Because of this lack of selectivity, it is impossible to draw firm conclusions about the role of any particular receptor in the clin. profile of the neuroleptic agents. Furthermore, the pharmacol. of potential human metabolites has to be taken into account in a proper anal. of the clin. profile. Consequently, most speculations on the key-target of clin. interesting antipsychotics (including clozapine) may be of little practical value. Clin. studies with receptor (subtype)-selective agents will be more informative.
AN 1995:560076 HCAPLUS <<LOGINID::20071023>>
DN 122:306430
TI Does the dopamine receptor subtype selectivity of antipsychotic agents provide useful leads for the development of novel therapeutic agents?
AU Hacksell, Uli; Jackson, David M.; Mohell, Nina
CS Astra Arcus AB, Preclinical R and D, Soedertaelje, S-151 85, Swed.
SO Pharmacology & Toxicology (Copenhagen) (1995), 76(5), 320-4
CODEN: PHTOEH; ISSN: 0901-9928
PB Munksgaard
DT Journal
LA English

L10 ANSWER 24 OF 24 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Biphasic displacement of [3H]YM-09151-2 binding in the rat brain by thioridazine, risperidone and clozapine, but not by other antipsychotics
AB The radioligand [3H]YM-09151-2 ((±)-cis-N-(1-benzyl-2-methylpyrrolidin-3-yl)-5-chloro-2-methoxy-4-methylamino benzamide) was used to study the binding of various antipsychotic agents. Saturation expts. showed that [3H]YM-09151-2 labeled a single population of binding sites in both the olfactory tubercle and the striatum (dissociation consts. (KD): 36 ± 3 pM and 26 ± 2 pM, resp.). The total number of binding sites (Bmax) was greater in the striatum than in the olfactory tubercle (18.1 ± 1.8 fmol/mg tissue and 5.3 ± 0.9 fmol/mg tissue resp.). Risperidone and thioridazine displaced [3H]YM-09151-2 in a biphasic manner in both brain regions, and clozapine also produced biphasic displacement curves in the olfactory tubercle but not in the striatum. All other dopamine D2 receptor antagonists tested displaced [3H]YM-09151-2 in a monophasic manner in both brain regions, in agreement with previously published data. Biphasic displacement did not appear to result from interactions with either the dopamine D3, dopamine D4, 5-HT2, 5-HT1C or the 5-HT1A receptor binding sites. It is suggested that thioridazine, risperidone and clozapine might discriminate between different affinity states and/or subtypes of the dopamine D2 receptor which may be different from the recently identified D2short and D2long receptors.
AN 1993:531414 HCAPLUS <<LOGINID::20071023>>

DN 119:131414
TI Biphasic displacement of [3H]YM-09151-2 binding in the rat brain by thioridazine, risperidone and clozapine, but not by other antipsychotics
AU Assie, Marie Bernadette; Sleight, Andrew J.; Koek, Wouter
CS Neurobiol. Div. II, Cent. Rech. Pierre Fabre, Castres, 81100, Fr.
SO European Journal of Pharmacology (1993), 237(2-3), 183-9
    CODEN: EJPHAZ; ISSN: 0014-2999
DT Journal
LA English

=> d his

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L3   1 S OLANZAPINE/CN
L4   1 S L3
L5   1 S ZIPRASIDONE/CN
L6   1 S ARIPIPRAZOLE/CN

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     FILE 'HCAPLUS' ENTERED AT 14:48:40 ON 23 OCT 2007
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L9   65 S L7 AND L8
L10   24 S L9 AND (PY<2003 OR AY<2003 OR PRY<2003)

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     FILE 'HCAPLUS' ENTERED AT 14:48:57 ON 23 OCT 2007

     FILE 'STNGUIDE' ENTERED AT 14:48:58 ON 23 OCT 2007

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FULL ESTIMATED COST                                       0.06     124.74

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CA SUBSCRIBER PRICE                                       0.00     -18.72

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FULL ESTIMATED COST                                       0.12     124.80

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CA SUBSCRIBER PRICE                                       0.00     -18.72

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=> s l2 and l8

           925 L2
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CA SUBSCRIBER PRICE                                       0.00     -18.72

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L13 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN

TI Schizophrenia: genesis, receptorology and current therapeutics

AB A review. Schizophrenia is a debilitating mental disease affecting approx. 1% of the population worldwide. Since the discovery of the first modern treatment for schizophrenia, chlorpromazine, in 1952 there have been many new structures investigated, only a small fraction of which have resulted in clin. useful drugs. Of these, haloperidol may be regarded as the drug for first line treatment. Since then, clozapine has emerged as the benchmark therapeutic ameliorating pos. and neg. symptoms and devoid of movement disorders, with its greatest feature being improvement of treatment-resistant patients. However, a major, potential lethal side-effect of clozapine is the induction of agranulocytosis, a blood disorder with unknown mechanism that results in lowered white-blood cell counts and consequent susceptibility to infections. In the 50 yr of antipsychotic drug development, several novel theories have evolved that focus on receptor sub-types (serotonin 5-HT2A, dopamine D2 and D4) and the degree to which they need to be selectively attenuated by the drugs. Also of significance is the location of these receptors in the brain in relation to the disease state, the myriad of side-effects associated with antipsychotics and physicochem. properties of antipsychotic mols. relative to models of the drugs and the GPCR receptors involved. The techniques for investigation have shown increasing sophistication and refinement over this period, involving cloned receptors and PET scanning for determination of receptor location, d. and binding, and rate consts. at receptors. Knowledge of receptor structure, although in its infancy since no membrane bound CNS-receptor has yet been crystallized, is likely to benefit substantially with advances in computer-aided modeling. Overall, these new techniques have resulted in a number of novel antipsychotics such as risperidone, sertindole, olanzapine, seroquel, zotepine and ziprasidone, whose design, synthesis and testing has benefited enormously from the accumulated knowledge base of the past 50 yr. In this review, we will provide a comprehensive update of the theories of action and clin. profiles of the latest drugs listed. The following appraisal of the literature will provide the practising medicinal chemist interested in this critical area of research with sufficient insight and understanding, to embark on productive investigations into the design and development of new therapeutic agents devoid of clin. limiting side-effects.

AN 2002:275553 HCAPLUS <<LOGINID::20071023>>
DN 137:163110
TI Schizophrenia: genesis, receptorology and current therapeutics
AU Capuano, B.; Crosby, I. T.; Lloyd, E. J.
CS Department of Medicinal Chemistry, Victorian College of Pharmacy, Monash University, Parkville, 3052, Australia
SO Current Medicinal Chemistry (2002), 9(5), 521-548
CODEN: CMCHE7; ISSN: 0929-8673
PB Bentham Science Publishers
DT Journal; General Review
LA English
RE.CNT 286 THERE ARE 286 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Ziprasidone: a novel antipsychotic agent with a unique human receptor binding profile
AB Ziprasidone is a novel antipsychotic agent with a unique combination of pharmacol. activities at human receptors. Ziprasidone has high affinity for human 5-HT receptors and for human dopamine D2 receptors. Ziprasidone is a 5-HT1A receptor agonist and an antagonist at 5-HT2A, 5-HT2C and 5-HT1B/1D receptors. Addnl., ziprasidone inhibits neuronal uptake of 5-HT and norepinephrine comparable to the antidepressant imipramine. This unique pharmacol. profile of ziprasidone may be related to its clin. effectiveness as a treatment for the pos., neg. and affective symptoms of schizophrenia with a low propensity for extrapyramidal side effects, cognitive deficits and weight gain.
AN 2001:609740 HCAPLUS <<LOGINID::20071023>>
DN 136:477
TI Ziprasidone: a novel antipsychotic agent with a unique human receptor binding profile
AU Schmidt, A. W.; Lebel, L. A.; Howard, H. R.; Zorn, S. H.
CS Groton Laboratories, CNS Discovery, Pfizer Global Research and Development, Groton, CT, 06340-1596, USA
SO European Journal of Pharmacology (2001), 425(3), 197-201
CODEN: EJPHAZ; ISSN: 0014-2999
PB Elsevier Science B.V.
DT Journal
LA English
RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Long-term effects of olanzapine, risperidone, and quetiapine on dopamine receptor types in regions of rat brain: implications for antipsychotic drug treatment
AB Changes in members of the dopamine (DA) D1-like (D1, D5) and D2-like (D2, D3, D4) receptor families in rat forebrain regions were compared by quant. in vitro receptor autoradiog. after prolonged treatment (28 days) with the atypical antipsychotics olanzapine, risperidone, and quetiapine. Olanzapine and risperidone, but not quetiapine, significantly increased D2 binding in medial prefrontal cortex (MPC; 67% and 34%), caudate-putamen (CPu; average 42%, 25%), nucleus accumbens (NAc; 37%, 28%), and hippocampus (HIP; 53%, 30%). Olanzapine and risperidone, but not quetiapine, produced even greater up-regulation of D4 receptors in CPu (61%, 37%), NAc (65%, 32%), and HIP (61%, 37%). D1-like and D3 receptors in all regions were unaltered by any treatment, suggesting their minimal role in mediating actions of these antipsychotics. The findings support the hypothesis that antipsychotic effects of olanzapine and risperidone are partly mediated by D2 receptors in MPC, NAc, or HIP, and perhaps D4 receptors in CPu, NAc, or HIP, but not in cerebral cortex. Selective up-regulation of D2 receptors by olanzapine and risperidone in CPu may reflect their ability to induce some extra-pyramidal effects. Inability of quetiapine to alter DA receptors suggests that non-dopaminergic mechanisms contribute to its

antipsychotic effects.
AN 2001:321641 HCAPLUS <<LOGINID::20071023>>
DN 135:132309
TI Long-term effects of olanzapine, risperidone, and quetiapine on dopamine receptor types in regions of rat brain: implications for antipsychotic drug treatment
AU Tarazi, Frank I.; Zhang, Kehong; Baldessarini, Ross J.
CS Mailman Research Center, McLean Division of Massachusetts General Hospital, Belmont, MA, USA
SO Journal of Pharmacology and Experimental Therapeutics (2001), 297(2), 711-717
CODEN: JPETAB; ISSN: 0022-3565
PB American Society for Pharmacology and Experimental Therapeutics
DT Journal
LA English
RE.CNT 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Characterization of dopaminergic compounds at hD2short, hD4.2 and hD4.7 receptors in agonist-stimulated [35S]GTPγS binding assays
AB Dopamine receptor agonists and antagonists have been extensively characterized in radioligand binding assays; only a limited number of labs. have characterized them using a functional assay at multiple receptor subtypes. Expts. were designed to assess four agonists and seven antagonists at three cloned human dopamine receptors using agonist-stimulated [35S]GTPγS binding assays in membranes to quantify the initial cellular event following ligand/receptor interaction. In this model there is constitutive G protein activity (agonist-independent [35S]GTPγS binding) and potentially constitutive dopamine receptor activity. Thus, discrimination between silent antagonists, partial agonists and inverse agonists is theor. possible. It was anticipated that distinctions could be made regarding efficacy of the seven receptor antagonists to provide insight regarding the therapeutic use of antipsychotic drugs.In membranes prepared from CHO cells transfected to express high densities of human D2short, D4.2 or D4.7 receptors, the dopamine receptor agonists apomorphine, pergolide, quinelorane and quinpirole produced concentration-dependent increases in agonist-stimulated [35S]GTPγS binding. At the hD2short receptor, pergolide and apomorphine were essentially equipotent and more potent than quinelorane and quinpirole; all four agonists displayed similar efficacy at this receptor. At the hD4.2 and the hD4.7 receptors apomorphine was the most potent and pergolide the least efficacious of the four drugs. The ability (both potency and efficacy) of clozapine, haloperidol, olanzapine, quetiapine, risperidone, spiperone and ziprasidone to block apomorphine-stimulated [35S]GTPγS binding and alter basal [35S]GTPγS binding was also assessed. All of the antagonists inhibited apomorphine-stimulated [35S]GTPγS binding with potencies (Kb values) similar to and in rank order consistent with their affinities reported in the literature using radioligand binding assays. Addnl., none of the antagonists altered basal, agonist-independent [35S]GTPγS binding, thus they behaved as pure, silent antagonists at D2short, D4.2 and D4.7 receptors under our conditions. In summary, the data suggest that therapeutic distinctions between typical and atypical antipsychotic drugs cannot be made based on their function at D2short, D4.2 and D4.7 subtypes of dopamine receptors.
AN 2000:295079 HCAPLUS <<LOGINID::20071023>>
DN 133:114944
TI Characterization of dopaminergic compounds at hD2short, hD4.2 and hD4.7 receptors in agonist-stimulated [35S]GTPγS binding assays
AU Gilliland, S. L.; Alper, R. H.
CS Toxicology and Therapeutics, Department of Pharmacology, University of Kansas Medical Center, Kansas City, KS, 66160-7417, USA
SO Naunyn-Schmiedeberg's Archives of Pharmacology (2000), 361(5),

498-504
CODEN: NSAPCC; ISSN: 0028-1298
PB Springer-Verlag
DT Journal
LA English
RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d l14 1-4 ti
YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS' - CONTINUE? (Y)/N:y

L14 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Schizophrenia: genesis, receptorology and current therapeutics

L14 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Ziprasidone: a novel antipsychotic agent with a unique human receptor binding profile

L14 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Long-term effects of olanzapine, risperidone, and quetiapine on dopamine receptor types in regions of rat brain: implications for antipsychotic drug treatment

L14 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Characterization of dopaminergic compounds at hD2short, hD4.2 and hD4.7 receptors in agonist-stimulated [35S]GTPγS binding assays

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COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
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http://www.cas.org/support/stngen/stndoc/properties.html

=> s aripiprazole/cn
L1            1 ARIPIPRAZOLE/CN

=> file stnguide
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FULL ESTIMATED COST                                         5.40       5.61

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=> file hcaplus
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
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FULL ESTIMATED COST                                         0.24       5.85

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FILE COVERS 1907 - 24 Oct 2007 VOL 147 ISS 18
FILE LAST UPDATED: 23 Oct 2007 (20071023/ED)

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=> s l1/thu

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          557 L1
       946710 THU/RL
L2        483 L1/THU
                (L1 (L) THU/RL)
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=> s depression or depressive or depressed

```
        84712 DEPRESSION
         9078 DEPRESSIVE
        66744 DEPRESSED
L3     144013 DEPRESSION OR DEPRESSIVE OR DEPRESSED
```

=> s smoking or nicotine or tobacco

```
        34188 SMOKING
        30279 NICOTINE
        82974 TOBACCO
L4     115763 SMOKING OR NICOTINE OR TOBACCO
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=> s antipsychotic or neuroleptic or ziprasidone or aripiprazole or olanzapine or claozapine or risperidone

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        10374 ANTIPSYCHOTIC
         7547 NEUROLEPTIC
          812 ZIPRASIDONE
          601 ARIPIPRAZOLE
         2490 OLANZAPINE
            0 CLAOZAPINE
         2766 RISPERIDONE
L5      18454 ANTIPSYCHOTIC OR NEUROLEPTIC OR ZIPRASIDONE OR ARIPIPRAZOLE OR
              OLANZAPINE OR CLAOZAPINE OR RISPERIDONE
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=> s antidepressant or fluoxetine or fluvoxamine or paroxetine or sertaline or SSRI or (selective serotonin reuptake)

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        21912 ANTIDEPRESSANT
         5986 FLUOXETINE
         1912 FLUVOXAMINE
         3318 PAROXETINE
            6 SERTALINE
         1755 SSRI
       440119 SELECTIVE
        72989 SEROTONIN
        10221 REUPTAKE
         3004 SELECTIVE SEROTONIN REUPTAKE
                (SELECTIVE(W)SEROTONIN(W)REUPTAKE)
L6      28127 ANTIDEPRESSANT OR FLUOXETINE OR FLUVOXAMINE OR PAROXETINE OR
              SERTALINE OR SSRI OR (SELECTIVE SEROTONIN REUPTAKE)
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=> s l2 and l3

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L7          78 L2 AND L3
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=> s l4 and l5 and l6

L8          82 L4 AND L5 AND L6

=> file stnguide

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=> file hcaplus
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
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FULL ESTIMATED COST                                         0.06       8.51

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FILE LAST UPDATED: 23 Oct 2007  (20071023/ED)

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 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> s l7 and (PY<2003 or AY<2003 or PRY<2003)

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       4465717 AY<2003
       3944520 PRY<2003
L9          14 L7 AND (PY<2003 OR AY<2003 OR PRY<2003)

=> s l8 and (PY<2003 or AY<2003 or PRY<2003)

      22908174 PY<2003
       4465717 AY<2003
       3944520 PRY<2003
L10         34 L8 AND (PY<2003 OR AY<2003 OR PRY<2003)

=> file stnguide

COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
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LAST RELOADED: Oct 19, 2007 (20071019/UP).

=> d l9 1-14 ti
YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS' - CONTINUE? (Y)/N:y

L9 ANSWER 1 OF 14 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Methods and compositions using cyclooxygenase 2 (COX-2) inhibitors for the treatment of psychiatric disorders, and combination therapies

L9 ANSWER 2 OF 14 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Adenosine A2a receptor antagonists for the treatment of extrapyramidal syndrome and other movement disorders

L9 ANSWER 3 OF 14 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Carbostyril derivatives and serotonin reuptake inhibitors for treatment of mood disorders

L9 ANSWER 4 OF 14 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Stereoisomers of p-hydroxy-milnacipran, and therapeutic use

L9 ANSWER 5 OF 14 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Antipsychotic combination therapies and compositions of an alpha-2 adrenergic receptor antagonist and an atypical antipsychotic neuroleptic

L9 ANSWER 6 OF 14 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Combination therapy for depression, prevention of suicide, and various medical and psychiatric conditions

L9 ANSWER 7 OF 14 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Methods and compositions using a cyclooxygenase 2 (COX-2) inhibitor for the treatment of psychiatric disorders

L9 ANSWER 8 OF 14 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Preparation of aripiprazole with low hygroscopicity

L9 ANSWER 9 OF 14 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Use of cyclooxygenase 2 (COX-2) inhibitors for the treatment of schizophrenia, delusional disorders, affective disorders, autism, or tic disorders

L9 ANSWER 10 OF 14 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Aripiprazole

L9 ANSWER 11 OF 14 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Carbostyril derivative 5-HT1a receptor subtype agonist for treatment of central nervous system disorders

L9 ANSWER 12 OF 14 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Carbostyril derivative 5-HT1a receptor agonists for treatment of central nervous system disorders

L9 ANSWER 13 OF 14 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Pharmaceuticals containing a combination of norepinephrine reuptake inhibitors and neuroleptics

L9 ANSWER 14 OF 14 HCAPLUS COPYRIGHT 2007 ACS on STN
TI The antipsychotic aripiprazole is a potent, partial agonist at the human 5-HT1A receptor

=> d l9 3 4 5 6 7 8 10 12 12 14 ti abs bib
YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS' - CONTINUE? (Y)/N:y

L9 ANSWER 3 OF 14 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Carbostyril derivatives and serotonin reuptake inhibitors for treatment of mood disorders
AB The pharmaceutical composition of the present invention comprises (1) a carbostyril derivative and (2) a serotonin reuptake inhibitor in a pharmaceutically acceptable carrier. The carbostyril derivative may be aripiprazole or a metabolite thereof, which is a dopamine-serotonin system stabilizer. The serotonin reuptake inhibitor may be fluoxetine, duloxetine, venlafaxine, milnacipran, citalopram, fluvoxamine, paroxetine, sertraline or escitalopram. The pharmaceutical composition of the present invention is useful for treating patients with mood disorders, particularly depression or major depressive disorder.
For example, a tablet formulation contained aripiprazole anhydride crystals B 5 mg, venlafaxine 75 mg, starch 131 mg, magnesium stearate 4 mg, and lactose 60 mg.
AN 2004:589419 HCAPLUS <<LOGINID::20071024>>
DN 141:128865
TI Carbostyril derivatives and serotonin reuptake inhibitors for treatment of mood disorders
IN Kikuchi, Tetsuro; Iwamoto, Taro; Hirose, Tsuyoshi
PA Otsuka Pharmaceutical Co., Ltd., Japan
SO PCT Int. Appl., 92 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004060374	A1	20040722	WO 2003-JP16724	20031225 <--
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
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	EP 1575590	A1	20050921	EP 2003-786308	20031225 <--
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	BR 2003017771	A	20051122	BR 2003-17771	20031225 <--
	CN 1726039	A	20060125	CN 2003-80106103	20031225 <--
	EP 1723957	A2	20061122	EP 2006-17539	20031225 <--
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	NZ 540054	A	20070928	NZ 2003-540054	20031225 <--
	JP 2004217650	A	20040805	JP 2003-433429	20031226 <--

	NO 2005002359	A	20050718	NO 2005-2359	20050512 <--
	ZA 2005003873	A	20060830	ZA 2005-3873	20050513 <--
	MX 2005PA06857	A	20050818	MX 2005-PA6857	20050622 <--
	IN 2005KN01229	A	20060630	IN 2005-KN1229	20050624 <--
	US 2006154938	A1	20060713	US 2005-540577	20051216 <--
PRAI	JP 2002-379003	A	20021227	<--	
	US 2003-470481P	P	20030514		
	CN 2003-80106103	A3	20031225		
	EP 2003-786308	A3	20031225		
	WO 2003-JP16724	W	20031225		

L9 ANSWER 4 OF 14 HCAPLUS COPYRIGHT 2007 ACS on STN

TI Stereoisomers of p-hydroxy-milnacipran, and therapeutic use

AB The invention relates generally to the enantiomers of p-hydroxymilnacipran or congeners thereof. Biol. assays revealed that racemic p-hydroxymilnacipran is approx. equipotent in inhibiting serotonin and norepinephrine uptake (IC50 = 28.6 nM for norepinephrine, IC50 = 21.7 nM for serotonin). Interestingly, (+)-p-hydroxymilnacipran is a more potent inhibitor of norepinephrine uptake than serotonin uptake (IC50 = 10.3 nM for norepinephrine, IC50 = 22 nM for serotonin). In contrast, (-)-p-hydroxymilnacipran is a more potent inhibitor of serotonin uptake compared to norepinephrine uptake (IC50 = 88.5 nM for norepinephrine, IC50 = 40.3 nM for serotonin). The invention also relates to salts and prodrug forms of the above compds. In certain embodiments, the compds. of the invention and a pharmaceutically acceptable excipient are combined to prepare a formulation for administration to a patient. Finally,the invention relates to methods of treating mammals suffering from various afflictions, e.g., depression, chronic pain, or fibromyalgia, comprising administering to a mammal in need thereof a therapeutically effective amount of a compound of the invention. Compound preparation is included.

AN 2004:392439 HCAPLUS <<LOGINID::20071024>>

DN 140:400095

TI Stereoisomers of p-hydroxy-milnacipran, and therapeutic use

IN Rariy, Roman V.; Heffernan, Michael; Buchwald, Stephen L.; Swager, Timothy M.

PA Collegium Pharmaceutical, Inc., USA

SO PCT Int. Appl., 163 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 6

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004039320	A2	20040513	WO 2003-US33681	20031022 <--
	WO 2004039320	A3	20040624		
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	AU 2003284342	A1	20040525	AU 2003-284342	20031022 <--
	US 2004142904	A1	20040722	US 2003-691465	20031022 <--
	US 7038085	B2	20060502		
	EP 1578719	A2	20050928	EP 2003-776524	20031022 <--
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     IN 2005CN01003        A     20070824    IN 2005-CN1003          20050524 <--
PRAI US 2002-421640P       P     20021025  <--
     US 2002-423062P       P     20021101  <--
     US 2003-445142P       P     20030205
     WO 2003-US33681       W     20031022
OS   MARPAT 140:400095

L9   ANSWER 5 OF 14  HCAPLUS  COPYRIGHT 2007 ACS on STN
TI   Antipsychotic combination therapies and compositions of an alpha-2
     adrenergic receptor antagonist and an atypical antipsychotic neuroleptic
AB   The invention provides novel antipsychotic therapies and compns. useful
     therein and provides methods for identifying new candidate mols. for the
     treatment of psychosis based on the proportional binding affinities for
     α2 adrenergic and D2 dopamine receptors.
AN   2004:101019  HCAPLUS <<LOGINID::20071024>>
DN   140:157473
TI   Antipsychotic combination therapies and compositions of an alpha-2
     adrenergic receptor antagonist and an atypical antipsychotic neuroleptic
IN   Pickar, David; Wadenberg, Marie-Louise; Svensson, Torgny
PA   Potomac, Pharma Inc., USA
SO   PCT Int. Appl., 45 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.            KIND   DATE        APPLICATION NO.         DATE
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PI   WO 2004011031          A1     20040205    WO 2003-US23440         20030728 <--
     WO 2004011031          A9     20040422
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             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
             PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
             TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
             FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     CA 2494109             A1     20040205    CA 2003-2494109         20030728 <--
     AU 2003259256          A1     20040216    AU 2003-259256          20030728 <--
     US 2004127489          A1     20040701    US 2003-629123          20030728 <--
     EP 1545618             A1     20050629    EP 2003-771917          20030728 <--
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             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
     JP 2005538108          T      20051215    JP 2004-524892          20030728 <--
     US 2006281735          A1     20061214    US 2006-405360          20060417 <--
PRAI US 2002-398718P        P      20020729  <--
     US 2002-398719P        P      20020729  <--
     US 2002-398720P        P      20020729  <--
     US 2002-402542P        P      20020812  <--
     US 2002-433781P        P      20021217  <--
     US 2002-433782P        P      20021217  <--
     US 2002-433785P        P      20021217  <--
     WO 2003-US23440        W      20030728
     US 2005-522699         A1     20050127
RE.CNT  3      THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
               ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9   ANSWER 6 OF 14  HCAPLUS  COPYRIGHT 2007 ACS on STN
TI   Combination therapy for depression, prevention of suicide, and
     various medical and psychiatric conditions
AB   The present invention relates to a new method of treatment for persons
```

meeting diagnoses for major depressive disorder, or other unipolar (non-bipolar, nonpsychotic and non-treatment resistant) depression. The method comprises administering a combination of two categories of drugs, antipsychotics or dopamine system stabilizers, in combination with a newer antidepressant such as a selective serotonin reuptake inhibitor, as initial treatment or as soon as possible. The method targets the prevention of suicide, and provides other benefits including preventing disease progression development of tolerance toward the antidepressants. Another aspect of the invention relates to using the method for alleviating cognitive distortion and related functional impairment or health risks, and/or using the method for smoking cessation or nicotine withdrawal.

AN 2004:100942 HCAPLUS <<LOGINID::20071024>>
DN 140:139528
TI Combination therapy for depression, prevention of suicide, and various medical and psychiatric conditions
IN Migaly, Peter
PA USA
SO PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004010932	A2	20040205	WO 2003-US23326	20030725 <--
	WO 2004010932	A3	20040722		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
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	CA 2529857	A1	20040205	CA 2003-2529857	20030725 <--
	AU 2003268026	A1	20040216	AU 2003-268026	20030725 <--
	US 2004204401	A1	20041014	US 2003-627358	20030725 <--
	EP 1551393	A2	20050713	EP 2003-748977	20030725 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	MX 2005PA00294	A	20050819	MX 2005-PA294	20050104 <--
PRAI	US 2002-319436P	P	20020730 <--		
	US 2003-627358	A	20030725		
	WO 2003-US23326	W	20030725		

L9 ANSWER 7 OF 14 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Methods and compositions using a cyclooxygenase 2 (COX-2) inhibitor for the treatment of psychiatric disorders
AB A method for the prevention, treatment, or inhibition of a psychiatric disorder, in particular schizophrenia, is described which comprises administering a COX-2 inhibitor, or prodrug thereof, to a subject. Moreover, a method for the prevention, treatment, or inhibition of a psychiatric disorder, in particular schizophrenia or a depressive disorder, is disclosed, comprising administering to a subject a COX-2 inhibitor or prodrug thereof in combination with a neuroleptic drug or an antidepressant. Compns. and kits that are suitable for the practice of the method are also described.
AN 2003:532347 HCAPLUS <<LOGINID::20071024>>
DN 139:79173
TI Methods and compositions using a cyclooxygenase 2 (COX-2) inhibitor for the treatment of psychiatric disorders

IN Muller, Norbert
PA Germany
SO U.S. Pat. Appl. Publ., 27 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003130334	A1	20030710	US 2002-157969	20020531 <--
	EP 1627639	A2	20060222	EP 2005-24864	20020531 <--
	EP 1627639	A3	20060927		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	US 2006167074	A1	20060727	US 2005-320757	20051230 <--
PRAI	DE 2001-10129328	A	20010619	<--	
	US 2002-364904P	P	20020314	<--	
	DE 2001-10129320	A	20010619	<--	
	EP 2002-738138	A3	20020531	<--	
	US 2002-157969	A2	20020531	<--	

OS MARPAT 139:79173

L9 ANSWER 8 OF 14 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Preparation of aripiprazole with low hygroscopicity
AB The present invention provides low hygroscopic forms of aripiprazole and processes for the preparation which will not convert to a hydrate or lose their original solubility even when a pharmaceutical containing the aripiprazole (anhydrous) crystals is stored for an extended period. Thus, aripiprazole hydrate was heated for 18 h at 100° and then for 3 h at 120° to produce the crystals of the anhydrous form of aripiprazole. A tablet formulation contained aripiprazole 5, starch 131, Mg stearate 4, and lactose 60 mg.
AN 2003:261676 HCAPLUS <<LOGINID::20071024>>
DN 138:276308
TI Preparation of aripiprazole with low hygroscopicity
IN Bando, Takuji; Aoki, Satoshi; Kawasaki, Junichi; Ishigami, Makoto; Taniguchi, Youichi; Yabuuchi, Tsuyoshi; Fujimoto, Kiyoshi; Nishioka, Yoshihiro; Kobayashi, Noriyuki; Fujimura, Tsutomu; Takahashi, Masanori; Abe, Kaoru; Nakagawa, Tomonori; Shinhama, Koichi; Utsumi, Naoto; Tominaga, Michiaki; Oi, Yoshihiro; Yamada, Shohei; Tomikawa, Kenji
PA Otsuka Pharmaceutical Co., Ltd., Japan
SO PCT Int. Appl., 174 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003026659	A1	20030403	WO 2002-JP9858	20020925 <--
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	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2379005	A1	20030325	CA 2002-2379005	20020327 <--
	CA 2426921	A1	20030403	CA 2002-2426921	20020925 <--
	AU 2002334413	A1	20030407	AU 2002-334413	20020925 <--
	BR 2002005391	A	20030729	BR 2002-5391	20020925 <--
	EP 1330249	A1	20030730	EP 2002-782507	20020925 <--

EP 1330249	B1	20060405			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK					
JP 2003212852	A	20030730	JP 2002-279085	20020925	<--
JP 3760264	B2	20060329			
CN 1463191	A	20031224	CN 2002-801754	20020925	<--
EP 1419776	A2	20040519	EP 2004-2427	20020925	<--
EP 1419776	A3	20040616			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK					
ZA 2003000113	A	20040806	ZA 2003-113	20020925	<--
AU 200234413	A	20041104	AU 2002-34413	20020925	<--
AU 2002334413	B2	20041104			
RU 2259366	C2	20050827	RU 2003-101334	20020925	<--
CN 1699346	A	20051123	CN 2005-10078599	20020925	<--
AT 322269	T	20060415	AT 2002-782507	20020925	<--
NZ 523313	A	20060526	NZ 2002-523313	20020925	<--
HU 2006000141	A2	20060529	HU 2006-141	20020925	<--
PT 1330249	T	20060630	PT 2002-782507	20020925	<--
RU 2279429	C2	20060710	RU 2004-126636	20020925	<--
CN 1817882	A	20060816	CN 2006-10006215	20020925	<--
ES 2261750	T3	20061116	ES 2002-2782507	20020925	<--
IN 2002KN01536	A	20050311	IN 2002-KN1536	20021217	<--
MX 2003PA00440	A	20031006	MX 2003-PA440	20030115	<--
US 2004058935	A1	20040325	US 2003-333244	20030616	<--
JP 2004256555	A	20040916	JP 2004-156130	20040526	<--
JP 3750023	B2	20060301			
JP 2006070045	A	20060316	JP 2005-341187	20051125	<--
US 2007202181	A1	20070830	US 2007-790605	20070426	<--
US 2007213343	A1	20070913	US 2007-790603	20070426	<--
US 2007212421	A1	20070913	US 2007-790604	20070426	<--
US 2007213344	A1	20070913	US 2007-790606	20070426	<--
US 2007203150	A1	20070830	US 2007-797019	20070430	<--
US 2007203151	A1	20070830	US 2007-797024	20070430	<--
US 2007203152	A1	20070830	US 2007-797030	20070430	<--
PRAI JP 2001-290645	A	20010925	<--		
JP 2001-348276	A	20011114	<--		
CA 2002-2379005	A	20020327	<--		
CN 2002-801754	A3	20020925	<--		
EP 2002-782507	A3	20020925	<--		
JP 2002-279085	A3	20020925	<--		
RU 2003-101334	A	20020925	<--		
WO 2002-JP9858	W	20020925	<--		
US 2003-333244	A3	20030616			

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 10 OF 14 HCAPLUS COPYRIGHT 2007 ACS on STN

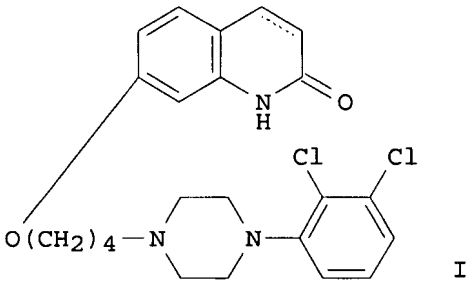
TI Aripiprazole

AB Aripiprazole is a quinolinone derivative and the first of a new class of atypical antipsychotics. The drug has partial agonist activity at dopamine D2 and serotonin 5-HT1A receptors, and is also an antagonist at 5-HT2A receptors. In patients with acute relapse of schizophrenia or schizoaffective disorder, aripiprazole 15 to 30 mg/day was at least as effective as haloperidol 10 mg/day and had similar efficacy to risperidone 6 mg/day in well designed, 4-wk, placebo-controlled trials. Neg. symptoms improved earlier in the aripiprazole than the risperidone group. Efficacy of aripiprazole was observed at week 1 in several trials and was sustained throughout the study periods. Aripiprazole was superior to placebo in a 26-wk trial in patients with stable, chronic schizophrenia. In a 52-wk trial involving patients with acute relapsing disease, aripiprazole was similar to haloperidol as assessed by time to failure to maintain response and was superior in ameliorating neg. and depressive symptoms. The incidence of extrapyramidal symptoms during aripiprazole therapy was

similar to that with risperidone and placebo but lower than with haloperidol. Compared with placebo, the proportion of patients with increased plasma prolactin levels and QTc prolongation was similar in patients treated with aripiprazole 15 to 30 mg/day but was significantly increased with haloperidol and risperidone.

AN 2002:892403 HCAPLUS <<LOGINID::20071024>>
DN 139:46891
TI Aripiprazole
AU McGavin, Jane K.; Goa, Karen L.
CS Adis International Limited, Auckland, N. Z.
SO CNS Drugs (2002), 16(11), 779-786
CODEN: CNDREF; ISSN: 1172-7047
PB Adis International Ltd.
DT Journal
LA English
RE.CNT 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 12 OF 14 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Carbostyril derivative 5-HT1a receptor agonists for treatment of central nervous system disorders
GI



I

AB The invention discloses the use of a compound for the production of a medicament for treating a patient suffering from a disorder of the central nervous system associated with 5-HT1a receptor subtype, the medicament including as an active ingredient a carbostyril derivative I (C-C bond between 3- and 4-positions in the carbostyril skeleton is single or double bond), or a pharmaceutically acceptable salt or solvate thereof.

AN 2002:594663 HCAPLUS <<LOGINID::20071024>>
DN 137:150248
TI Carbostyril derivative 5-HT1a receptor agonists for treatment of central nervous system disorders
IN Jordan, Shaun; Kikuchi, Tetsuro; Tottori, Katsura; Hirose, Tsuyoshi; Uwahodo, Yasufumi
PA Otsuka Pharmaceutical Co., Ltd., Japan; Otsuka Pharma Co Ltd
SO PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002060423	A2	20020808	WO 2002-JP626	20020129 <--
	WO 2002060423	A3	20030410		

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RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR

	CA 2429496	A1	20020808	CA 2002-2429496	20020129 <--
	AU 2002226752	A1	20020812	AU 2002-226752	20020129 <--
	EP 1355639	A2	20031029	EP 2002-716434	20020129 <--
	EP 1355639	B1	20060412		
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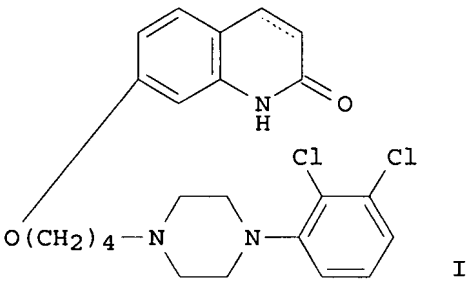
	BR 2002006237	A	20031223	BR 2002-6237	20020129 <--
	CN 1484524	A	20040324	CN 2002-803551	20020129 <--
	JP 2004517937	T	20040617	JP 2002-560616	20020129 <--
	EP 1621198	A2	20060201	EP 2005-23971	20020129 <--
	EP 1621198	A3	20060412		
	EP 1621198	B1	20070523		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR				
	AT 322894	T	20060415	AT 2002-716434	20020129 <--
	PT 1355639	T	20060630	PT 2002-716434	20020129 <--
	CN 1813745	A	20060809	CN 2005-10022828	20020129 <--
	EP 1712225	A1	20061018	EP 2006-15782	20020129 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR				
	ES 2261652	T3	20061116	ES 2002-2716434	20020129 <--
	CN 1879624	A	20061220	CN 2006-10094388	20020129 <--
	AT 362763	T	20070615	AT 2005-23971	20020129 <--
	IN 2003KN00722	A	20070914	IN 2003-KN722	20030604 <--
	MX 2003PA06603	A	20040212	MX 2003-PA6603	20030723 <--
	HK 1061805	A1	20060804	HK 2004-104847	20040706 <--
	AU 2005201772	A1	20050519	AU 2005-201772	20050427 <--
	AU 2005201772	B2	20070517		
	AU 2007201701	A1	20070510	AU 2007-201701	20070417
PRAI	US 2001-770210	A	20010129 <--		
	AU 2002-226752	A3	20020129 <--		
	CN 2002-803551	A3	20020129 <--		
	CN 2005-10022828	A3	20020129 <--		
	EP 2002-716434	A3	20020129 <--		
	EP 2005-23971	A3	20020129 <--		
	WO 2002-JP626	W	20020129 <--		
	AU 2005-201772	A3	20050427		

L9 ANSWER 12 OF 14 HCAPLUS COPYRIGHT 2007 ACS on STN

TI Carbostyril derivative 5-HT1a receptor agonists for treatment of central nervous system disorders

GI



I

AB The invention discloses the use of a compound for the production of a medicament
for treating a patient suffering from a disorder of the central nervous system associated with 5-HT1a receptor subtype, the medicament including as an active ingredient a carbostyril derivative I (C-C bond between 3- and 4-positions in the carbostyril skeleton is single or double bond), or a

pharmaceutically acceptable salt or solvate thereof.

AN 2002:594663 HCAPLUS <<LOGINID::20071024>>

DN 137:150248

TI Carbostyril derivative 5-HT1a receptor agonists for treatment of central nervous system disorders

IN Jordan, Shaun; Kikuchi, Tetsuro; Tottori, Katsura; Hirose, Tsuyoshi; Uwahodo, Yasufumi

PA Otsuka Pharmaceutical Co., Ltd., Japan; Otsuka Pharma Co Ltd

SO PCT Int. Appl., 31 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002060423	A2	20020808	WO 2002-JP626	20020129 <--
	WO 2002060423	A3	20030410		
	W: AU, BR, CA, CN, ID, IN, JP, KR, MX, PH, SG				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
	CA 2429496	A1	20020808	CA 2002-2429496	20020129 <--
	AU 2002226752	A1	20020812	AU 2002-226752	20020129 <--
	EP 1355639	A2	20031029	EP 2002-716434	20020129 <--
	EP 1355639	B1	20060412		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR				
	BR 2002006237	A	20031223	BR 2002-6237	20020129 <--
	CN 1484524	A	20040324	CN 2002-803551	20020129 <--
	JP 2004517937	T	20040617	JP 2002-560616	20020129 <--
	EP 1621198	A2	20060201	EP 2005-23971	20020129 <--
	EP 1621198	A3	20060412		
	EP 1621198	B1	20070523		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR				
	AT 322894	T	20060415	AT 2002-716434	20020129 <--
	PT 1355639	T	20060630	PT 2002-716434	20020129 <--
	CN 1813745	A	20060809	CN 2005-10022828	20020129 <--
	EP 1712225	A1	20061018	EP 2006-15782	20020129 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR				
	ES 2261652	T3	20061116	ES 2002-2716434	20020129 <--
	CN 1879624	A	20061220	CN 2006-10094388	20020129 <--
	AT 362763	T	20070615	AT 2005-23971	20020129 <--
	IN 2003KN00722	A	20070914	IN 2003-KN722	20030604 <--
	MX 2003PA06603	A	20040212	MX 2003-PA6603	20030723 <--
	HK 1061805	A1	20060804	HK 2004-104847	20040706 <--
	AU 2005201772	A1	20050519	AU 2005-201772	20050427 <--
	AU 2005201772	B2	20070517		
	AU 2007201701	A1	20070510	AU 2007-201701	20070417
PRAI	US 2001-770210	A	20010129 <--		
	AU 2002-226752	A3	20020129 <--		
	CN 2002-803551	A3	20020129 <--		
	CN 2005-10022828	A3	20020129 <--		
	EP 2002-716434	A3	20020129 <--		
	EP 2005-23971	A3	20020129 <--		
	WO 2002-JP626	W	20020129 <--		
	AU 2005-201772	A3	20050427		

L9 ANSWER 14 OF 14 HCAPLUS COPYRIGHT 2007 ACS on STN

TI The antipsychotic aripiprazole is a potent, partial agonist at the human 5-HT1A receptor

AB Aripiprazole, 7-{4-[4-(2,3-dichlorophenyl)-1-piperazinyl]butyloxy}-3,4-dihydro-2(1H)-quinolinone, a novel antipsychotic with partial agonist activity at dopamine D2 receptors, bound with high affinity to recombinant

human 5-HT1A receptors (h5-HT1A) in Chinese hamster ovary cell membranes and displayed potent, partial agonism at 5-HT1A receptors in a guanosine-5'-O-(3-[35S]thio)-triphosphate ([35S]GTPγS)-binding assay that was blocked completely by a selective 5-HT1A receptor antagonist. An interaction with 5-HT1A receptors may contribute to the overall efficacy of aripiprazole against symptoms of schizophrenia, including anxiety, depression, cognitive and neg. symptoms, and to its favorable side-effect profile. Combined with previous studies demonstrating the potent partial agonism of aripiprazole at dopamine D2 receptors, this study suggests aripiprazole is the first dopamine-serotonin system stabilizer.

AN 2002:440186 HCAPLUS <<LOGINID::20071024>>
DN 138:83213
TI The antipsychotic aripiprazole is a potent, partial agonist at the human 5-HT1A receptor
AU Jordan, Shaun; Koprivica, Vuk; Chen, Ruoyan; Tottori, Katsura; Kikuchi, Tetsuro; Altar, C. Anthony
CS Maryland Research Laboratories, Neuroscience Department, Otsuka Maryland Research Institute, Rockville, MD, 20850, USA
SO European Journal of Pharmacology (2002), 441(3), 137-140
CODEN: EJPHAZ; ISSN: 0014-2999
PB Elsevier Science B.V.
DT Journal
LA English
RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d l10 1-34 ti
YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS' - CONTINUE? (Y)/N:y

L10 ANSWER 1 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Transdermal delivery of systemically active central nervous system drugs

L10 ANSWER 2 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Synergistic pharmaceutical compositions containing olanzapine and analgetic drugs

L10 ANSWER 3 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Therapeutic placebo enhancement of commonly used medications

L10 ANSWER 4 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Pharmaceutical compositions for prevention of overdose or abuse

L10 ANSWER 5 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Method of using a cyclooxygenase 2 (COX-2) inhibitor and a 5-HT1A receptor modulator as a combination therapy for pain, inflammation, and other conditions

L10 ANSWER 6 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Combination therapy for depression, prevention of suicide, and various medical and psychiatric conditions

L10 ANSWER 7 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Methods for treating depression and other CNS disorders using enantiomerically enriched desmethyl- and didesmethyl- metabolites of citalopram

L10 ANSWER 8 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Collegium Internationale Neuro-Psychopharmacologicum (C.I.N.P.): XXIIIrd congress: Montreal, Canada, 23-27 June 2002

L10 ANSWER 9 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Molecular Properties That Influence the Oral Bioavailability of Drug Candidates

L10 ANSWER 10 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Preparation of dihydroimidazo[2,1-b]thiazoles and dihydro-5H-thiazolo[3,2-a]pyrimidines with 5-HT receptor affinity

L10 ANSWER 11 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Curative method for pathologic syndromes and homeopathic medicinal preparations

L10 ANSWER 12 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Transdermal or transmucosal dosage forms containing nicotine for smoking cessation

L10 ANSWER 13 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Smoking in patients receiving psychotropic medications: A pharmacokinetic perspective

L10 ANSWER 14 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Methods of determining individual hypersensitivity to a pharmaceutical agent from gene expression profile

L10 ANSWER 15 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Methods and compositions for the treatment of neuroleptic and related disorders using sertindole derivatives

L10 ANSWER 16 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Compositions and methods for improved delivery of ionizable hydrophobic therapeutic agents

L10 ANSWER 17 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
TI QSAR model for drug human oral bioavailability. [Erratum to document cited in CA133:159633]

L10 ANSWER 18 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Analysis of urine for drugs of abuse using mixed-mode solid-phase extraction and gas chromatography-mass spectrometry

L10 ANSWER 19 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
TI QSAR Model for Drug Human Oral Bioavailability

L10 ANSWER 20 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Extractableness of relevant toxicological compounds with 1-chlorbutane

L10 ANSWER 21 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Preparation of substituted benzopyran derivatives as anticonvulsants

L10 ANSWER 22 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Olanzapine: pharmacokinetic and pharmacodynamic profile

L10 ANSWER 23 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Preparation of substituted isoquinolines as anticonvulsants

L10 ANSWER 24 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Preparation of substituted isoquinolinyl ureas as anticonvulsants

L10 ANSWER 25 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Metabolic bioactivation reactions potentially related to drug toxicities

L10 ANSWER 26 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Preparation of heteroaryloxy alkanamines having effects on serotonin-related systems

L10 ANSWER 27 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Polymorphic drug oxidation: Relevance to the treatment of psychiatric disorders

L10 ANSWER 28 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Capillary zone electrophoresis in a comprehensive screen for basic drugs in whole blood

L10 ANSWER 29 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Bicyclic compounds, including benzopyrans, with pharmaceutical activity

L10 ANSWER 30 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
TI preparation of cholecystokinin analogs containing α-substituted amino acids as appetite suppressants

L10 ANSWER 31 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Drugs abused by humans preferentially increase synaptic dopamine concentrations in the mesolimbic system of freely moving rats

L10 ANSWER 32 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Antinicotinic effects of drugs with clinically useful sedative-antianxiety properties

L10 ANSWER 33 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Cataleptic state and hypothermia in mice, caused by central cholinergic stimulation and antagonized by anticholinergic and antidepressant drugs

L10 ANSWER 34 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Relation of psychological drugs to the adrenergic and cholinergic systems

=> d l10 2 5 7 10 12 13 1521 22 29 31 32 33 ti abs bib
YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS' - CONTINUE? (Y)/N:n

=> d l10 2 5 7 10 12 13 15 21 22 29 31 32 33 ti abs bib
YOU HAVE REQUESTED DATA FROM FILE 'HCAPLUS' - CONTINUE? (Y)/N:y

L10 ANSWER 2 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Synergistic pharmaceutical compositions containing olanzapine and analgetic drugs
AB The subject of the invention is a pharmaceutical product, which contains olanzapine or its medically acceptable salt and one or more pain relieving active ingredients. The product according to the invention has a synergetic effect. Thus tablets were prepared from a composition (weight parts):
hydroxypropyl cellulose 4.0; olanzapine 1.18; ibuprofen 3.0; lactose 79.32; Crospovidon 5; cellulose 10; magnesium stearate 0.5. The tablets were coated with a mixture of hydroxypropyl methylcellulose, polyethylene glycol, polysorbat 80 and titania.
AN 2007:265980 HCAPLUS <<LOGINID::20071024>>
DN 146:448301
TI Synergistic pharmaceutical compositions containing olanzapine and analgetic drugs
IN Shannon, Harlan E.; Womer, Daniel E.
PA USA
SO Hung. Pat. Appl., 38pp.
CODEN: HUXXCV
DT Patent
LA Hungarian

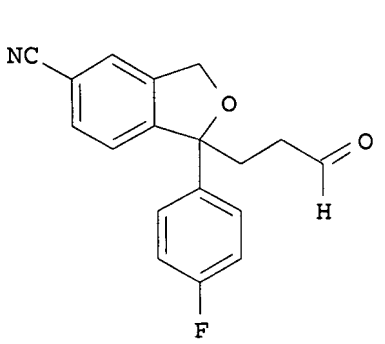
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	HU 9903375	A2	20000228	HU 1999-3375	19970324 <--
	HU 9903375	A3	20000428		
PRAI	HU 1999-3375		19970324 <--		

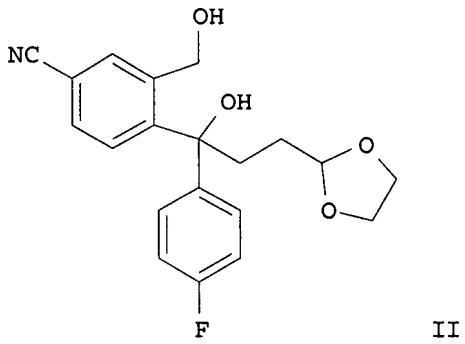
L10 ANSWER 5 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Method of using a cyclooxygenase 2 (COX-2) inhibitor and a 5-HT1A receptor modulator as a combination therapy for pain, inflammation, and other conditions
AB Compns. and methods to treat or prevent pain, inflammation, or inflammation-related disorder, as well as a neurol. disorder involving neurodegeneration involve a combination of a COX-2 inhibitor and a 5-HT1A receptor modulator.
AN 2004:452952 HCAPLUS <<LOGINID::20071024>>
DN 141:1296
TI Method of using a cyclooxygenase 2 (COX-2) inhibitor and a 5-HT1A receptor modulator as a combination therapy for pain, inflammation, and other conditions
IN Stephenson, Diane T.; Taylor, Duncan P.
PA Pharmacia Corporation, USA
SO PCT Int. Appl., 195 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004045509	A2	20040603	WO 2003-US35739	20031111 <--
	WO 2004045509	A3	20040826		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2004147581	A1	20040729	US 2003-702403	20031105 <--
	AU 2003295431	A1	20040615	AU 2003-295431	20031111 <--
PRAI	US 2002-427198P	P	20021118 <--		
	WO 2003-US35739	W	20031111		

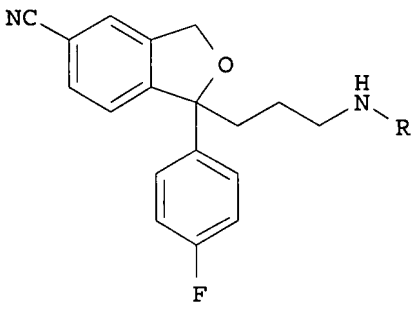
L10 ANSWER 7 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Methods for treating depression and other CNS disorders using enantiomerically enriched desmethyl- and didesmethyl- metabolites of citalopram
GI



I



II



III

AB This invention relates to the preparation of I and II and derivs. of I and II in their racemic, enantiomerically enriched, or optically pure forms. This invention further relates to novel compns. of matter containing enantiomerically enriched (-)-desmethylcitalopram (-)-III (R = Me), (+)-didesmethylcitalopram (+)-III (R = Me), or (-)-didesmethylcitalopram (-)-III (R = H) or mixts. thereof in optimal ratios. Contrary to prior teachings, the enantiomerically enriched citalopram metabolites disclosed herein possess potent serotonin reuptake inhibitory activity, with minimal inhibitory effects on the reuptake of other known monoamines, e.g., norepinephrine (NE) or dopamine (DA). For example, stepwise reaction of 1-oxo-1,3-dihydroisobenzofuran-5-carbonitrile with 4-fluorophenylmagnesium bromide and the chiral Grignard reagent, which was prepared from 2-(2-bromoethyl)-[1,3]dioxolane and Mg powder, in THF gave II. Cyclization using mesyl chloride in CH_2Cl_2, followed by reduction provided the I. Reaction of the aldehyde with (-)-tert-butylsulfinamide in the presence of $Ti(OEt)_4$ in EtOH afforded the sulfinamide, which was reduced to the amine III (R = H) with 10% HCl in MeOH. Protection of the amine with BOC anhydride in the presence of TEA in CH_2Cl_2 provided the enantiomerically enriched isomers, which were separated on a chiral column and subsequently deprotected with TFA to give (+)-III (R = H) and (-)-III (R = H). In biol. assays, (-)-III (R = H) and (+)-III (R = H) strongly inhibited serotonergic 5-HT receptor activity with Ki values of 5.8 nM and 90 nM, resp., with little effect on NE and DA transporter activity. By comparison, racemic citalopram inhibited serotonin reuptake with a Ki of 3.9 nM. The present invention also discloses methods for treating disorders, dysfunctions and diseases for which inhibition of serotonin reuptake is therapeutically beneficial. In particular, the present invention discloses a method for treating various forms of depression and other CNS disorders with pharmaceutical compns. described herein.

AN 2003:376842 HCAPLUS <<LOGINID::20071024>>

DN 138:385297

TI Methods for treating depression and other CNS disorders using enantiomerically enriched desmethyl- and didesmethyl- metabolites of citalopram

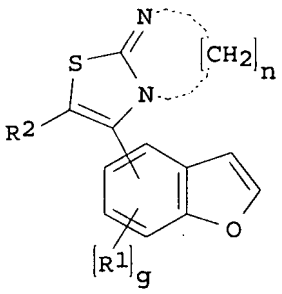
IN Bush, Larry R.; Currie, Mark G.; Senanayake, Chris H.; Fang, Kevin Q.

PA Sepracor, Inc., USA
SO PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

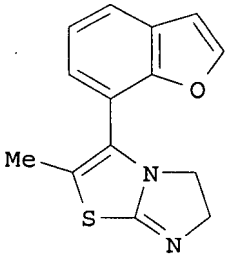
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003040121	A1	20030515	WO 2002-US35408	20021105 <--
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2465186	A1	20030515	CA 2002-2465186	20021105 <--
	AU 2002356903	A1	20030519	AU 2002-356903	20021105 <--
	AU 2002356903	A2	20030519		
	EP 1446396	A1	20040818	EP 2002-802848	20021105 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
	BR 2002013949	A	20040831	BR 2002-13949	20021105 <--
	HU 2004001934	A2	20050128	HU 2004-1934	20021105 <--
	HU 2004001934	A3	20070529		
	JP 2005510518	T	20050421	JP 2003-542167	20021105 <--
	CN 1705654	A	20051207	CN 2002-822084	20021105 <--
	NZ 532478	A	20070223	NZ 2002-532478	20021105 <--
	IN 2004KN00505	A	20060616	IN 2004-KN505	20040419 <--
	ZA 2004003409	A	20051026	ZA 2004-3409	20040505 <--
	MX 2004PA04368	A	20040811	MX 2004-PA4368	20040507 <--
	US 2004266864	A1	20041230	US 2004-842055	20040507 <--
	NO 2004002013	A	20040514	NO 2004-2013	20040514 <--
PRAI	US 2001-337608P	P	20011108	<--	
	WO 2002-US35408	W	20021105	<--	

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 10 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Preparation of dihydroimidazo[2,1-b]thiazoles and dihydro-5H-thiazolo[3,2-a]pyrimidines with 5-HT receptor affinity
GI



I



II

AB The title compds. [I; g = 0-5; n = 2-3; R1 = halo, alkyl, alkoxy, etc.; R2

= H, alkyl, hydroxyalkyl, etc.; the condensed thiazole ring is attached at the 4,5,6 or 7-position of the benzofuran ring] which have affinity for 5-HT1A receptors and which inhibit neuronal re-uptake of 5-hydroxytryptamine and/or noradrenaline, to processes for their preparation, to pharmaceutical compns. containing them and to their use in the treatment of depression, anxiety, psychoses (for example schizophrenia), tardive dyskinesia, obesity, drug addiction, drug abuse, cognitive disorders, Alzheimer's disease, obsessive-compulsive behavior, panic attacks, social phobias, eating disorders such as bulimia, anorexia, snacking and binge eating, non-insulin dependent diabetes mellitus, hyperglycemia, hyperlipidemia, stress, as an aid to smoking cessation and in the treatment and/or prophylaxis of seizures, neurol. disorders such as epilepsy and/or conditions in which there is neurol. damage such as stroke, brain trauma, cerebral ischemia, head injuries and hemorrhage, were prepared and formulated. Thus, treating 1-(benzo[b]furan-7-yl)propan-1-one (preparation given) with phenyltrimethylammonium tribromide in THF followed by reaction of the intermediate with 2-imidazolidinethione in the presence of AcOH in EtOH afforded II.HBr which showed Ki of 28 nM against 5-HT1A binding.

AN 2002:256267 HCAPLUS <<LOGINID::20071024>>
DN 136:279473
TI Preparation of dihydroimidazo[2,1-b]thiazoles and dihydro-5H-thiazolo[3,2-a]pyrimidines with 5-HT receptor affinity
IN Brough, Paul; Watts, John Paul; Cockroft, Victor; Kerrigan, Frank; Doyle, Kevin James
PA Knoll G.m.b.H., Germany
SO PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002026747	A1	20020404	WO 2001-GB4317	20010927 <--
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2001090126	A5	20020408	AU 2001-90126	20010927 <--
PRAI	GB 2000-23610	A	20000927 <--		
	WO 2001-GB4317	W	20010927 <--		

OS MARPAT 136:279473
RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 12 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Transdermal or transmucosal dosage forms containing nicotine for smoking cessation
AB A transdermal or transmucosal pharmaceutical for the treatment of nicotine dependence or to the smoking cessation contains nicotine, nicotine salt, nicotine derivative or a material with nicotinergic effect, in combination with another drug affecting the central nervous system.
AN 2001:780323 HCAPLUS <<LOGINID::20071024>>
DN 135:335142
TI Transdermal or transmucosal dosage forms containing nicotine for smoking cessation
IN Theobald, Frank; Frick, Ulrich
PA LTS Lohmann Therapie-Systeme A.-G., Germany

SO Ger. Offen., 6 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 10018834	A1	20011025	DE 2000-10018834	20000415 <--
	WO 2001080837	A2	20011101	WO 2001-EP3712	20010402 <--
	WO 2001080837	A3	20020221		
	W: AU, BR, CA, CN, CZ, HU, IL, IN, JP, KR, MX, NZ, PL, RU, TR, US, ZA				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
	CA 2404581	A1	20020926	CA 2001-2404581	20010402 <--
	EP 1274405	A2	20030115	EP 2001-929488	20010402 <--
	EP 1274405	B1	20040602		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR				
	HU 2003000048	A2	20030628	HU 2003-48	20010402 <--
	BR 2001010060	A	20030715	BR 2001-10060	20010402 <--
	JP 2004501090	T	20040115	JP 2001-577936	20010402 <--
	AT 268168	T	20040615	AT 2001-929488	20010402 <--
	ES 2220772	T3	20041216	ES 2001-1929488	20010402 <--
	NZ 521155	A	20060224	NZ 2001-521155	20010402 <--
	RU 2301671	C2	20070627	RU 2002-123887	20010402 <--
	ZA 2002006758	A	20031001	ZA 2002-6758	20020823 <--
	MX 2002PA09104	A	20030312	MX 2002-PA9104	20020918 <--
	IN 2002DN00977	A	20050128	IN 2002-DN977	20021001 <--
	US 2003049308	A1	20030313	US 2002-257564	20021015 <--
	HK 1051495	A1	20041126	HK 2003-103650	20030523 <--
PRAI	DE 2000-10018834	A	20000415 <--		
	WO 2001-EP3712	W	20010402 <--		

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 13 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Smoking in patients receiving psychotropic medications: A pharmacokinetic perspective
AB A review with refs. Many psychiatric patients smoke, and are believed to be heavier smokers than those without psychiatric disorders. Cigarette smoking is one of the environmental factors that contributes to interindividual variations in response to an administered drug. Polycyclic aromatic hydrocarbons (PAHs) present in cigarette smoke induce hepatic aryl hydrocarbon hydroxylases, thereby increasing metabolic clearance of drugs that are substrates for these enzymes. PAHs have been shown to induce 3 hepatic cytochrome P 450 (CYP) isoenzymes, primarily CYP1A1, 1A2 and 2E1. Drug therapy can also be affected pharmacodynamically by nicotine. The most common effect of smoking on drug disposition in humans is an increase in biotransformation rate, consistent with induction of drug-metabolizing enzymes. Induction of hepatic enzymes has been shown to increase the metabolism and to decrease the plasma concns. of imipramine, clomipramine, fluvoxamine and trazodone. The effect of smoking on the plasma concns. of amitriptyline and nortriptyline is variable. Amfebutamone (bupropion) does not appear to be affected by cigarette smoking. Smoking is associated with increased clearance of tiotixene, fluphenazine, haloperidol and olanzapine. Plasma concns. of chlorpromazine and clozapine are reduced by cigarette smoking. Clin., reduced drowsiness in smokers receiving chlorpromazine, and benzodiazepines, compared with non-smokers has been reported. Increased clearance of the benzodiazepines alprazolam, lorazepam, oxazepam, diazepam and demethyl-diazepam is found in cigarette smokers, whereas chlordiazepoxide does not appear to be affected by smoking. Carbamazepine appears to be minimally affected by

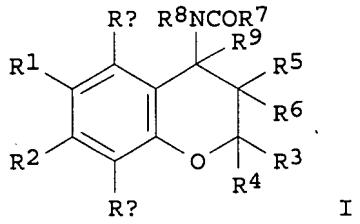
cigarette smoke, perhaps because hepatic enzymes are already stimulated by its own autoinductive properties. Cigarette smoking can affect the pharmacokinetic and pharmacodynamic properties of many psychotropic drugs. Clinicians should consider smoking as an important factor in the disposition of these drugs.

AN 2001:547621 HCAPLUS <<LOGINID::20071024>>
DN 135:314505
TI Smoking in patients receiving psychotropic medications: A pharmacokinetic perspective
AU Desai, Hiral D.; Seabolt, Julia; Jann, Michael W.
CS Department of Pharmacy Practice and Pharmaceutical Sciences, Southern School of Pharmacy, Mercer University, Atlanta, GA, USA
SO CNS Drugs (2001), 15(6), 469-494
CODEN: CNDREF; ISSN: 1172-7047
PB Adis International Ltd.
DT Journal; General Review
LA English
RE.CNT 94 THERE ARE 94 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 15 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Methods and compositions for the treatment of neuroleptic and related disorders using sertindole derivatives
AB The invention relates to novel methods using, and pharmaceutical compns. and dosage forms comprising, sertindole derivs. Sertindole derivs. include, but are not limited to, nor-sertindole, 5-oxo-sertindole, dehydro-sertindole, and dehydro-nor-sertindole. The methods of the invention are directed to the treatment and prevention of neuroleptic and related disorders such as, but are not limited to, psychotic disorders, depression, anxiety, substance addiction, memory impairment and pain. For example, capsules were prepared containing a sertindole derivative 50.0 mg, lactose 48.5 mg, TiO2 0.5 mg, and Mg stearate 1.0 mg.
AN 2000:861482 HCAPLUS <<LOGINID::20071024>>
DN 134:32977
TI Methods and compositions for the treatment of neuroleptic and related disorders using sertindole derivatives
IN Jerussi, Thomas P.
PA Sepracor Inc., USA
SO PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000072837	A2	20001207	WO 2000-US14984	20000531 <--
	WO 2000072837	A3	20010517		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 6489341	B1	20021203	US 2000-580492	20000530 <--
PRAI	US 1999-137447P	P	19990602 <--		
	US 2000-580492	A	20000530 <--		

L10 ANSWER 21 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Preparation of substituted benzopyran derivatives as anticonvulsants
GI



I

AB The title anti-convulsant compds. [I; R1 = alkylcarbonyl in which alkyl is substituted by OH; R2 = H, cycloalkyl, alkyl, etc.; Ra = H, halo, NO2, etc.; Rb = H, halo, NO2, etc.; one of R3 and R4 = H or alkyl and the other = alkyl, CF3, CH2Xa (Xa = F, Cl, Br, etc.); R3R4 together = (un)substituted by alkyl polymethylene; R5 = alkylcarbonyloxy, PhCO2, ONO2, PhCH2O, PhO, alkoxy and R6 and R9 = H or R5 = OH and R6 and R9 = H, alkyl; R7 = (un)substituted heteroaryl, Ph; R8 = H, alkyl, OH, etc.; R7R8 together = alkylene and R8NCOR7 is cis or trans to the R5], potentially useful in the treatment and/or prevention of anxiety, mania, depression, panic disorders and/or aggression, disorders associated with a subarachnoid hemorrhage or neural shock, the effects associated with withdrawal from substances of abuse such as cocaine, nicotine, alc. and benzodiazepines, disorders treatable and/or preventable with anti-convulsive agents, such as epilepsy including post-traumatic epilepsy, Parkinson's disease, psychosis, migraine, cerebral ischemia, Alzheimer's disease and other degenerative diseases, etc., were prepared Thus, treatment of (3R,4S)-6-acetyl-4-(3,5-difluorobenzamido)-3,4-dihydro-2,2-dimethyl-3-hydroxy-2H-1-benzopyran with bis[(trifluoroacetoxy)iodo]benzene and F3CCO2H in MeCN/H2O afforded 36% (3R,4S)-I [R1 = HOCH2CO; R2 = H; Ra = Rb = H; R3 = R4 = Me; R5 = OH; R6 = H; R7 = 3,5-F2C6H3; R8 = R9 = H] which showed an increase in seizure threshold relative to control of 317% at 1 mg/kg (tested 30 min post dosing to rats).

AN 2000:15193 HCAPLUS <<LOGINID::20071024>>
DN 132:64171
TI Preparation of substituted benzopyran derivatives as anticonvulsants
IN Bell, David; Cox, Peter J.; Thompson, Mervyn; Turner, Gillian
PA Smithkline Beecham Plc, UK
SO PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000000484	A1	20000106	WO 1999-GB2000	19990625 <--
	W: CA, JP, US				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	CA 2335846	A1	20000106	CA 1999-2335846	19990625 <--
	EP 1091950	A1	20010418	EP 1999-926667	19990625 <--
	EP 1091950	B1	20030409		
	R: BE, CH, DE, ES, FR, GB, IT, LI, NL				
	JP 2002519347	T	20020702	JP 2000-557245	19990625 <--
	ES 2197645	T3	20040101	ES 1999-926667	19990625 <--
	US 6395909	B1	20020528	US 2000-720019	20001219 <--
PRAI	GB 1998-13949	A	19980629 <--		
	WO 1999-GB2000	W	19990625 <--		

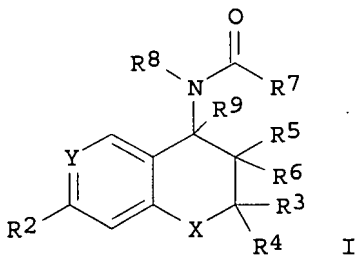
OS MARPAT 132:64171

RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

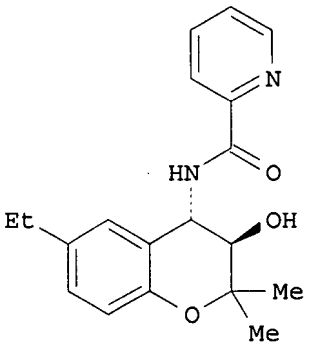
L10 ANSWER 22 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Olanzapine: pharmacokinetic and pharmacodynamic profile
AB A review with 56 refs. Multicenter trials in patients with schizophrenia confirm that olanzapine is a novel antipsychotic agent with broad efficacy, eliciting a response in both the pos. and neg. symptoms of schizophrenia. Compared with traditional antipsychotic agents, olanzapine causes a lower incidence of extrapyramidal symptoms and minimal perturbation of prolactin levels. Generally, olanzapine is well tolerated. The pharmacokinetics of olanzapine are linear and dose-proportional within the approved dosage range. Its mean half-life in healthy individuals is 33 h, ranging 21-54 h. The mean apparent plasma clearance is 26 L/h, ranging 12-47 L/h. Smokers and men have a higher clearance of olanzapine than women and nonsmokers. After administering [14C] olanzapine, approx. 60% of the radioactivity is excreted in urine and 30% in feces. Olanzapine is predominantly bound to albumin (90%) and α1-acid glycoprotein (77%). Olanzapine is metabolized to its 10- and 4'- N-glucuronides, 4'-N-demethylolanzapine [cytochrome P 450 (CYP) 1A2] and olanzapine N-oxide (flavin monooxygenase 3). Metabolism to 2-hydroxymethylolanzapine via CYP2D6 is a minor pathway. The 10-N-glucuronide is the most abundant metabolite, but formation of 4'-N-demethylolanzapine is correlated with the clearance of olanzapine. Olanzapine does not inhibit CYP isoenzymes. No clin. significant metabolic interactions have been found between olanzapine and diazepam, EtOH, imipramine, R/S-warfarin, aminophylline, biperiden, lithium or fluoxetine. Fluvoxamine, an inhibitor of CYP1A2, increases plasma concns. of olanzapine; inducers of CYP1A2, including tobacco smoke and carbamazepine, decrease olanzapine concns. Orthostatic changes have been observed when olanzapine and diazepam or alc. were coadministered. Pharmacodynamic interactions occur between olanzapine and alc., and olanzapine and imipramine, implying that patients should avoid operating hazardous equipment or driving an automobile while experiencing the short-term effects of the combinations. Individual factors with the largest impact on olanzapine pharmacokinetics are gender and smoking status. The plasma clearance of olanzapine generally varies over a 4-fold range, but the variability in the clearance and concentration of olanzapine does not appear to be associated with the severity or duration of adverse effects or the degree of efficacy. Thus, dosage adjustments appear unnecessary for these individual factors. However, dosage modification should be considered for patients characterized by a combination of factors associated with decreased oxidative metabolism, for example, debilitated or elderly women who are nonsmokers.
AN 1999:656821 HCAPLUS <<LOGINID::20071024>>
DN 131:266443
TI Olanzapine: pharmacokinetic and pharmacodynamic profile
AU Callaghan, John T.; Bergstrom, Richard F.; Ptak, Louis R.; Beasley, Charles M.
CS Lilly Laboratory for Clinical Research, Indiana University Hospital and Outpatient Center, Indianapolis, IN, USA
SO Clinical Pharmacokinetics (1999), 37(3), 177-193
CODEN: CPKNDH; ISSN: 0312-5963
PB Adis International Ltd.
DT Journal; General Review
LA English
RE.CNT 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 29 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Bicyclic compounds, including benzopyrans, with pharmaceutical activity

GI



I



II

AB Use of title compds. I and their pharmaceutically acceptable salts for manufacture of drugs for treatment and/or prophylaxis of disorders resulting from subarachnoid hemorrhage, neural shock, cerebral ischemia, Parkinson's disease, migraine, and/or psychosis is claimed [wherein either Y = N and R2 = H, or Y = CR1, wherein either (1) one of R1 and R2 = H and the other = H or any of a wide variety of substituents, or (2) one of R1 and R2 = NO2, cyano, or alkylcarbonyl, and the other = OMe, (di)(alkyl)amino, alkanoylamino; or (3) R1R2 = (CH2)4, CH:CHCH:CH, or atoms to form (un)substituted triazole or oxadiazole ring; one of R3 and R4 = H or alkyl, and the other = alkyl, CF3, various monosubstituted Me groups (e.g., halomethyl); either (1) R5 = alkylcarbonyloxy, OBz, ONO2, OCH2Ph, OPh, or alkoxy, and R6 = R9 = H, or (2) R5 = OH, R6 = H or alkyl, and R9 = H; R7 = (un)substituted Ph or heteroaryl; R8 = H, alkyl, OR9, NHCOR10; R9 = H, alkyl, CHO, alkanoyl, aroyl, aralkyl; R10 = H, alkyl, alkoxy, (di)(alkyl)amino, aminoalkyl, (hetero)aryl, etc.; X = O, NR11; R11 = H, alkyl; R5 is trans to NR8COR7 group]. Use of a similar set of compds. for manufacturing drugs for therapy of anxiety, mania, depression, substance withdrawal, convulsions, and epilepsy is also claimed. A variety of tests are described, and results for a few compds. in the anticonvulsant and antiischemic tests are given. A list of 68 individual compds. I, most of which are novel, is given, and methods for their synthesis are either described or referenced. For example, amidation of picolinic acid with trans-4S-amino-3,4-dihydro-2,2-dimethyl-2H-1-benzopyran-3R-ol [as the D-(-)-mandelate salt] gave title compound II. Three compds. I gave 44-154% increases in seizure threshold at 30 mg/kg orally in the maximal electroshock test in mice.

AN 1995:408400 HCAPLUS <<LOGINID::20071024>>
DN 122:187394
TI Bicyclic compounds, including benzopyrans, with pharmaceutical activity
IN Thompson, Mervyn; Evans, John Morris; Upton, Neil; Chan, Wai Ngor; Vong, Kuok Keong; Willette, Robert Nicholas
PA Smithkline Beecham PLC, UK; Smithkline Beecham Corp.
SO PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9413656	A1	19940623	WO 1993-GB2512	19931208 <--

W: AT, AU, BB, BG, BR, BY, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, LV, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, UZ, VN

RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE,
BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

CA	2151515	A1	19940623	CA 1993-2151515	19931208 <--
AU	9456557	A	19940704	AU 1994-56557	19931208 <--
AU	679475	B2	19970703		
EP	673373	A1	19950927	EP 1994-902044	19931208 <--

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE

JP	08505132	T	19960604	JP 1993-513934	19931208 <--
JP	2003137880	A	20030514	JP 2002-260175	19931208 <--
ZA	9309238	A	19941014	ZA 1993-9238	19931209 <--
CN	1094613	A	19941109	CN 1993-121686	19931210 <--
CN	1066625	B	20010606		
US	5908860	A	19990601	US 1995-448518	19950706 <--
CN	1227099	A	19990901	CN 1998-126100	19981224 <--
CN	1270169	A	20001018	CN 1999-124893	19991119 <--
PRAI GB	1992-25881	A	19921211 <--		
GB	1992-25956	A	19921211 <--		
GB	1992-25957	A	19921211 <--		
GB	1992-25963	A	19921211 <--		
GB	1992-25964	A	19921211 <--		
JP	1994-513934	A3	19931208 <--		
WO	1993-GB2512	W	19931208 <--		

OS MARPAT 122:187394

L10 ANSWER 31 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Drugs abused by humans preferentially increase synaptic dopamine concentrations in the mesolimbic system of freely moving rats
AB The effect of various drugs on the extracellular concentration of dopamine in 2 terminal dopaminergic areas, the nucleus accumbens septi (a limbic area) and the dorsal caudate nucleus (a subcortical motor area), was studied in freely moving rats by using brain dialysis. Drugs abused by humans (e.g., opiates, ethanol, nicotine, amphetamine, and cocaine) increased extracellular dopamine concns. in both areas, especially in the accumbens, and elicited hypermotility at low doses. On the other hand, drugs with aversive properties (e.g., agonists of κ opioid receptors, U-50,488, tifluadom, and bremazocine) reduced dopamine release in the accumbens and in the caudate and elicited hypomotility. Haloperidol, a neuroleptic drug, increased extracellular dopamine concns., but this effect was not preferential for the accumbens and was associated with hypomotility and sedation. Drugs not abused by humans [e.g., imipramine (an antidepressant), atropine (an antimuscarinic drug), and diphenhydramine (an antihistamine) failed to modify synaptic dopamine concns. These results provide biochem. evidence for the hypothesis that stimulation of dopaminergic neurotransmission in the limbic system might be a fundamental property of drugs that are abused.
AN 1988:504610 HCAPLUS <<LOGINID::20071024>>
DN 109:104610
TI Drugs abused by humans preferentially increase synaptic dopamine concentrations in the mesolimbic system of freely moving rats
AU Di Chiara, Gaetano; Imperato, Assunta
CS Inst. Exp. Pharmacol. Toxicol., Univ. Cagliari, Cagliari, 09100, Italy
SO Proceedings of the National Academy of Sciences of the United States of America (1988), 85(14), 5274-8
CODEN: PNASA6; ISSN: 0027-8424
DT Journal
LA English

L10 ANSWER 32 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Antinicotinic effects of drugs with clinically useful sedative-antianxiety properties
GI For diagram(s), see printed CA Issue.
AB Mice were given a drug orally and 2 hr later were challenged with an i.v. LD95 of (-)-nicotine bitartrate [65-31-6]. Amitriptyline-HCl [549-18-8], imipramine-HCl [113-52-0], doxepin-HCl [1229-29-4],

meprobamate [57-53-4], chlordiazepoxide-HCl [438-41-5], diazepam [439-14-5], trifluoroperazine-2HCl [440-17-5], haloperidol [52-86-8], thioridazine-HCl [130-61-0], chlorpromazine-HCl [69-09-0], phenobarbital sodium (I) [57-30-7], propranolol-HCl [318-98-9], and diphenylhydantoin [57-41-0] were all active in protecting mice from extensor convulsions and lethality. Iproniazid phosphate [305-33-9], tranylcypromine sulfate [13492-01-8], atropine sulfate [55-48-1], benztropine methanesulfonate [132-17-2] and trimethadione [127-48-0] were inactive. There appears to be a relation between blockage of nicotine-induced extensor convulsions and lethality in mice and sedative-antianxiety effects in man. This relation is especially good for drugs designated as antidepressant , antianxiety and antipsychotic.

AN 1976:364 HCAPLUS <<LOGINID::20071024>>
DN 84:364
TI Antinicotinic effects of drugs with clinically useful sedative-antianxiety properties
AU Aceto, Mario D.
CS Dep. Pharmacol., Med. Coll. Virginia, Richmond, VA, USA
SO Pharmacology (1975), 13(5), 458-64
CODEN: PHMGBN; ISSN: 0031-7012
DT Journal
LA English

L10 ANSWER 33 OF 34 HCAPLUS COPYRIGHT 2007 ACS on STN
TI Cataleptic state and hypothermia in mice, caused by central cholinergic stimulation and antagonized by anticholinergic and antidepressant drugs
AB A cataleptic state was produced in mice by arecoline (20 mg./kg., i.p.), pilocarpine (8 mg./kg., i.p.), tremorine (6 mg./kg., i.p.), nicotine (7 mg./kg., i.p.), and para-oxon (1 mg./kg., s.c.). To protect the animals against the peripheral actions of these cholinergics, atropine methylnitrate (5 mg./kg., s.c.) was given before the first 3 drugs, hexamethonium bromide (5 mg./kg., i.p.) before nicotine, and pralidoxime (75 mg./kg., s.c.) before para-oxon. Atropine, scopolamine, imipramine, desipramine, and amitriptyline prevented catalepsy. This antagonistic action was dose-dependent, scopolamine being at least 10-fold more active than atropine. Desipramine was less active than imipramine. With the exception of nicotine, cataleptic doses of the cholinergics also caused hypothermia, which was diminished or abolished by atropine and scopolamine, the latter being, however, inactive against tremorine hypothermia. Anticataleptic doses of the antidepressants did not influence hypothermia. Muscarinic stimulation of the central nervous system causes catalepsy and can cause hypothermia, and catalepsy and hypothermia are independent phenomena. 62 references.
AN 1968:458277 HCAPLUS <<LOGINID::20071024>>
DN 69:58277
OREF 69:10871a,10874a
TI Cataleptic state and hypothermia in mice, caused by central cholinergic stimulation and antagonized by anticholinergic and antidepressant drugs
AU Zetler, G.
CS Inst. Pharmakol., Med. Akad. Luebeck, Luebeck, Fed. Rep. Ger.
SO International Journal of Neuropharmacology (1968), 7(4), 325-35
CODEN: IJNEAQ; ISSN: 0375-9458
DT Journal
LA English